90 F.4th 357
United States Court of Appeals, Fifth Circuit.

WAGES AND WHITE LION INVESTMENTS, L.L.C., doing business as Triton Distribution, Petitioner,
v.
FOOD & DRUG ADMINISTRATION, Respondent,
Wages and White Lion Investments, L.L.C., doing business as Triton Distribution; Vapetasia, L.L.C., Petitioners,
v.
Food & Drug Administration, Respondent.

No. 21-60766
|
consolidated with No. 21-60800
|
FILED January 3, 2024

Synopsis

Background: Manufacturers of flavored e-cigarette products petitioned for review of Food and Drug Administration's (FDA) orders denying manufacturers' premarket tobacco applications (PMTA).

Holdings: The Court of Appeals, en banc, Oldham, Circuit Judge, held that:

FDA engaged in prohibited post hoc rationalizations;

FDA violated the fair notice doctrine;

FDA arbitrarily and capriciously changed its position without acknowledgement or explanation;

manufacturers acted in good faith reliance on FDA's pre-decisional guidance; and

FDA's capriciousness could not be forgiven as harmless.

Petitions granted, order set aside, and matters remanded.

Haynes, Circuit Judge, filed dissenting opinion in which Stewart, Southwick, Higginson, and Douglas, Circuit Judges, joined.

Graves, Circuit Judge, joined the dissent in part, and filed opinion.

Procedural Posture(s): Review of Administrative Decision.

***361** Appeal from the Food & Drug Administration, Agency Nos. 21 USC 3871, PM0003531

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Before Richman, Chief Judge, and Jones, Smith, Stewart, Elrod, Southwick, Haynes, Graves, Higginson, Willett, Ho, Duncan, Engelhardt, Oldham, Wilson, and Douglas, Circuit Judges. *

* JUDGE RAMIREZ joined the court after this case was submitted and did not participate in the decision.

Opinion

Andrew S. Oldham, Circuit Judge, joined by Richman, Chief Judge, and Jones, Smith, Elrod, Willett, Ho, Duncan, Engelhardt, and Wilson, Circuit Judges:

***362** Over several years, the Food and Drug Administration ("FDA") sent manufacturers of flavored e-cigarette products on a wild goose chase.

First, the agency gave manufacturers detailed instructions for what information federal regulators needed to approve e-cigarette products. Just as importantly, FDA gave manufacturers specific instructions on what regulators did *not* need. The agency said manufacturers' marketing plans would be "critical" to the success of their applications. And the agency promulgated hundreds of pages of guidance documents, hosted public meetings, and posted formal presentations to its website—all with the (false) promise that a flavored-product manufacturer *could*, at least in theory, satisfy FDA's instructions. The regulated manufacturers dutifully spent untold millions conforming their behavior and their applications to FDA's say-so.

Then, months after receiving hundreds of thousands of applications predicated on its instructions, FDA turned around, pretended it never gave anyone any instructions about anything, imposed new testing requirements without any notice, and denied all one million flavored e-cigarette applications for failing to predict the agency's *volte face.* Worse, after telling manufacturers that their marketing plans were "critical" to their applications, FDA candidly admitted that it did not read a single word of the one million plans. Then FDA denied that its voluminous guidance documents and years-long instructional processes meant anything. Why? Because, the agency said, it always reserved the implied power to ignore every instruction it ever gave and to require the very studies it said could be omitted, along with the secret power to not even read the marketing plans it previously said were "critical." It was the regulatory equivalent of Romeo sending Mercutio on a wild goose chase—and then admitting there never was a goose while denying he even suggested the chase. *Cf.* WILLIAM SHAKESPEARE, ROMEO AND JULIET act 2, sc. 4.

FDA justifies its behavior with two principal arguments. First, FDA argues that its years' worth of regulatory guidance was not worth the paper it was printed on because it was hedged with cautious qualifiers and never *guaranteed* that any particular submission would be granted. Second, and most disturbingly, FDA argues that its capriciousness should be forgiven as harmless because the agency promises to deny petitioners' applications even if we remand to make the agency follow the law.

Today we reject both propositions. As the Supreme Court recently reminded us: "If men must turn square corners when they deal with the government, it cannot be too much to expect the government to turn square corners when it deals with them." *Niz-Chavez v. Garland*, 593 U.S. 155, 172, 141 S.Ct. 1474, 209 L.Ed.2d 433 (2021). No principle is more important when considering how the unelected administrators of the Fourth Branch of Government treat the American people. And FDA's regulatory switcheroos in this case ***363** bear no resemblance to square corners. As for the agency's harmless-error argument, the Supreme Court recently, unanimously, and summarily rejected it. *Calcutt v. FDIC*, 598 U.S. 623, 143 S.Ct. 1317, 215 L.Ed.2d 557 (2023) (per curiam). We do the same here with the expectation that FDA will give petitioners the benefit of a full and fair regulatory proceeding on remand, notwithstanding its prior promises to reject their applications no matter what.

I.

A.

In 2009, Congress enacted the Family Smoking Prevention and Tobacco Control Act ("TCA") to regulate tobacco products. *See*21 U.S.C. §§ 387 *et seq.* The TCA prohibits manufacturers from selling any "new tobacco product" without authorization from FDA. *See id.* § 387j(a); *id.* § 387a(b) (delegating to FDA the authority to determine what constitutes new tobacco products). In 2016, FDA deemed e-cigarettes and their component parts [1] to be "new tobacco products." Deeming Tobacco Products To Be Subject to the Federal Food, Drug, and Cosmetic Act, 81 Fed. Reg. 28,973 (May 10, 2016) ("Deeming Rule"). The upshot: E-cigarette manufacturers had to submit premarket tobacco applications ("PMTAs") for FDA approval to sell their products. *See id.* at 28,977.

1 The briefs and record materials in this case use a dizzying array of different terms to refer to e-cigarettes and their component parts: electronic cigarettes, e-cigarettes, electronic nicotine delivery devices ("ENDS"), nicotine cartridges, vaping products, vape pens, e-liquids, e-juice, and others. Unless context dictates otherwise, we refer to this list collectively as "e-cigarettes" throughout this opinion.

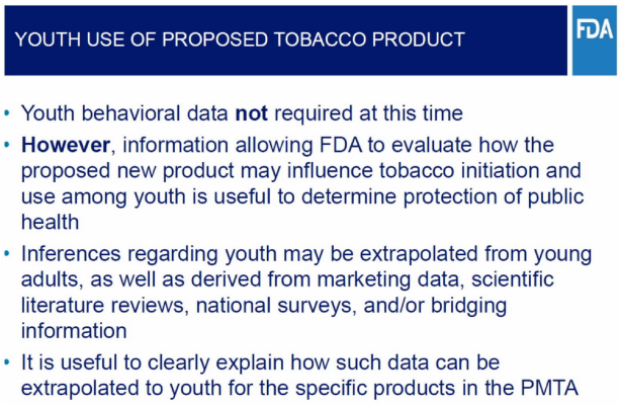
The TCA directs FDA to review the PMTAs to determine whether "permitting such tobacco product to be marketed would be appropriate for the protection of the public health." 21 U.S.C. § 387j(c)(2)(A). In making this determination, FDA must consider "the risks and benefits to the population as a whole." *Id.* § 387j(c)(4). This includes considering (1) the "increased or decreased likelihood that existing users of tobacco products will stop using such products" and (2) "the increased or decreased likelihood that those who do not use tobacco products will start using such products." *Id.* § 387j(c)(4)(A)–(B).

FDA then undertook to clarify these standards. The agency first announced that it would extend the PMTA compliance deadlines for several years so the agency could promulgate application instructions and the manufacturers could comply with them. *See* FDA, GUIDANCE FOR INDUSTRY, EXTENSION OF CERTAIN TOBACCO PRODUCT COMPLIANCE DEADLINES RELATED TO THE FINAL DEEMING RULE 5–11 (Aug. 10, 2017), https://perma.cc/WC42-ALYD ("Deadline Guidance"). [2]

2 FDA originally set the PMTA deadline as August 8, 2022. *See* Deadline Guidance at 8. A district court in Maryland ordered FDA to shorten it. FDA complied with that order, later extended the deadline because of COVID, and eventually settled on a PMTA deadline of September 9, 2020. *See Vapor Tech. Ass'n v. FDA*, 977 F.3d 496, 497–502 (6th Cir. 2020) (summarizing shifting deadlines).

FDA provided its instructions on five relevant occasions. Warning: the detail that follows might be mind-numbing. But FDA's detailed instructions are important to explain what e-cigarette manufacturers understood FDA would require of them. These details are important to understand why every single e-cigarette manufacturer in the entire Nation behaved just as petitioners did. And these details are important to explain why FDA cannot now pretend ***364** that it gave the regulated community fair notice of the PMTA requirements.

1. First, at a public meeting in October 2018, FDA stated in a formal presentation still available for download on the agency's website: "*No specific studies are required for a PMTA*; it may be possible to support a marketing order for an ENDS product without conducting new nonclinical or clinical studies given other data sources can support the PMTA." FDA, PREMARKET TOBACCO PRODUCT APPLICATION CONTENT OVERVIEW 26 (Oct. 23, 2018), https://perma.cc/BV8D-HR7H ("October 2018 Guidance") (emphasis added). FDA recommended that applicants "[c]ompare the new tobacco product to a representative sample of tobacco products on the market (i.e., either grandfathered or with marketing authorization)" and "[i]nclude justification for why using evidence or data from other products is appropriate." *Id.* at 11. And regarding the question of youth use, FDA published this slide:



Id. at 18.

2. Second, in June 2019, FDA promulgated a 52-page, single-spaced guidance document entitled "Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems: Guidance for Industry." A.284 ("June 2019 Guidance"). In it, FDA assured manufacturers that they need not perform long-term studies or submit long-term data in their PMTAs: "Given the relatively new entrance of [e-cigarettes] on the U.S. market ... limited data may exist from scientific studies and analyses.... *Nonetheless, in general, FDA does not expect that applicants will need to conduct long-term studies to support an application.*" A.298–99 (emphasis added) (footnote omitted); *see also* A.317 (same).

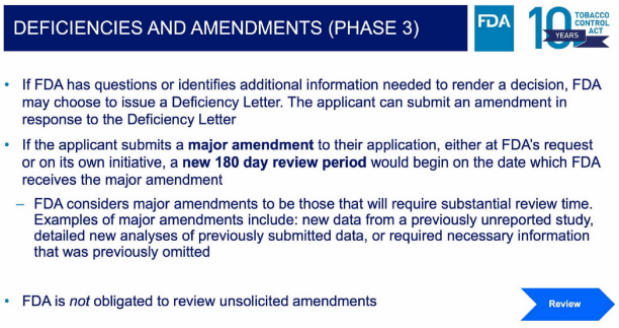
Rather, FDA specifically pointed to surveys as the kind of data that could support PMTAs: "Although randomized clinical trials could address cessation behavior of users of tobacco products, FDA believes this would also be true for observational studies (perception, actual use, or both) examining cessation behaviors." A.324. "Observational studies" include surveys. Petrs' EB Br. 9.

In the same guidance document, FDA also directed manufacturers to produce copious ***365** data about their marketing plans. As one of many examples of FDA's marketing-plan directives, the agency said:

> FDA also recommends sharing your marketing plan to enable FDA to better understand the potential consumer demographic. In addition, and if the product is currently marketed, FDA recommends sharing sales data broken down by population demographics and tobacco use status. Sales data, if available, should be analyzed in regular (preferably 4-week or monthly) intervals and should include:
>
> • The Universal Product Code that corresponds to the product(s) identified in the PMTA;
>
> • Total U.S. sales reported in dollars, units, and volume with breakdowns by U.S. census region, major retail markets, and channels in which the product is sold (e.g., convenience stores, food and drug markets, big box retailers, internet/online sales, tobacco specialty shops) [*sic*] promotional discounts (e.g., buy-one-get-one free or percentage discount);
>
> • Demographic characteristics of product(s) purchasers, such as age, gender, and tobacco use status; and
>
> • Information on top selling brands as a comparison for all recommended information, if available, so FDA can assess the market for the PMTA product to better estimate the potential impact on public health.

A.325 (quotation omitted) (footnote omitted).

3. Third, at a public meeting in October 2019, FDA again published a formal presentation. Again, the presentation remains available on FDA's website. FDA, PREMARKET TOBACCO PRODUCT APPLICATION (PMTA) REVIEW PATHWAY 20 (Oct. 28–29, 2019), https://perma.cc/9S7Z-JQX8 ("October 2019 Guidance"). In that presentation, FDA told e-cigarette manufacturers how the agency intended to review and act upon PMTAs. Among other things, FDA stated:



Id. at 20. And FDA assured manufacturers that "[a] decision w[ould] be made on each specific product, not the submission" as a whole. *Id.* at 21. At the same meeting, FDA again told manufacturers what it expected to see regarding youth vaping: Manufacturers should "address how they are going to restrict youth access and youth use.... [W]hat are their marketing plans[?] What are the age verification ***366** plans[?] I mean these are some of the kinds of things that you might want to take time to describe in your application to ensure to FDA that your product will not ... exacerbate

the current situation in methods to curb and improve limiting youth access." A.347.

4. Fourth, in September 2019, FDA issued a proposed rule governing PMTAs that reiterated that FDA did "not expect that long-term clinical studies (i.e., those lasting approximately 6 months or longer) [would] need to be conducted for each PMTA." Premarket Tobacco Product Applications and Recordkeeping Requirements, 84 Fed. Reg. 50,566, 50,619 (Sept. 25, 2019) ("PMTA Proposed Rule").

Instead, FDA said that manufacturers' "marketing plans" were "*critical*" to the success of their PMTAs. *Id.* at 50,581 (emphasis added). And FDA focused manufacturers' attention on those plans in painstaking detail:

> The applicant's marketing plans will help FDA determine whether permitting the marketing of the new tobacco product would be APPH ["appropriate for the protection of public health," 21 U.S.C. § 387j(c)(2)(A)] because they will provide input that is critical to FDA's determination of the likelihood of changes in tobacco product use behavior, especially when considered in conjunction with other information contained in the application. FDA will review the marketing plan to evaluate potential youth access to, and youth exposure to the labeling, advertising, marketing, or promotion of, a new tobacco product. For example, heavy use of online social media to promote a tobacco product without access restrictions, as opposed to actions such as paper mailings directed only to current smokers of legal age, indicates the potential for youth to be exposed to the promotion of the product. This information would help FDA make its APPH determination by showing whether a PMTA fully or accurately accounts for the likelihood of changes in tobacco product use behavior that may occur as a result of marketing the new tobacco product. For example, if the PMTA does not address youth access to the product, youth exposure to the product's labeling, advertising, marketing, and promotion, and youth initiation, such as describing how it proposes to restrict the sale or distribution of its product to limit potential youth access to the product (e.g., selling the tobacco product in adult-only establishments) or exposure to advertising (e.g., using age verification controls for digital advertising), FDA may be unable to determine that the applicant has made a showing that permitting the marketing of the new tobacco product would be APPH.

Id. at 50,581.

5. Fifth, in January 2020, FDA issued a 30-page, single-spaced enforcement guidance document entitled "Enforcement Priorities for Electronic Nicotine Delivery Systems (ENDS) and Other Deemed Products on the Market Without Premarket Authorization." A.185 ("2020 Enforcement Guidance"). [3] In this guidance document, FDA stated that after the PMTA deadline in September 2020, it would prioritize enforcement resources against "flavored, cartridge-based ENDS products (other than a tobacco-or menthol-flavored ENDS product)." A.186.

3 FDA issued this guidance in January 2020 and revised it in April 2020 due to the extension of the PMTA submission deadline. *See* Petrs' EB Br. 12 n.3; *supra* n.2.

What is a "flavored" e-cigarette product? As used in FDA's guidance documents and the parties' briefs, "flavored" e-cigarettes have flavors like blueberry, strawberry, ***367** and cherry, as well as various branded flavors like "Kauai Kolada," "Margarita Mixer," and "Mandarin Mint." *E.g.*, A.247. The term "flavored" does *not* include e-cigarettes that taste like tobacco or menthol. A.186.

What is a "cartridge-based" product? As used in FDA's guidance, a "cartridge-based" product "consists of, includes, or involves a cartridge or pod that holds liquid that is to be aerosolized through product use. For purposes of this definition, a cartridge or pod is any small, enclosed unit (sealed or unsealed) designed to fit within or operate as part of an electronic nicotine delivery system." A.192. These include e-cigarettes commonly known as "vape pens." The pen holds a small cartridge or pod, which is often but not always disposable, with a nicotine solution that a user vaporizes and inhales. Designs and styles vary, but cartridge-based products are generally smaller and lighter than open tank products that must be refilled with nicotine liquid by the user. *See, e.g.*, CDC, E-CIGARETTE, OR VAPING, PRODUCTS VISUAL DICTIONARY 9–12, https://perma.cc/5QD9-52NQ (last visited Dec. 21, 2023) ("CDC Visual Dictionary").

In its 2020 Enforcement Guidance, FDA explained in detail why it was focused on cartridge-based e-cigarettes. FDA stated:

> Of particular concern are the design features that appear to

> make the cartridge-based products so popular with young people. Attributes typically present in cartridge-based products include a relatively small size that allows for easy concealability, and intuitive and convenient features that facilitate ease of use, including draw activation, prefilled cartridges or pods, and USB rechargeability.

A.199. FDA explained that cartridge-based products are small, and hence can be more easily concealed at school or in social circumstances where youth need to hide them. *See ibid.* And many popular cartridge-based vaping pens have batteries that are recharged via USB ports and hence "blend in with other equipment" that youth might innocently possess. *Ibid.* Moreover, cartridge-based products are ready for immediate use, have no settings to adjust, have no tanks that need to be refilled, and require little or no assembly—all design features that make them more attractive to youth vapers. *See* A.199–200. Open tank systems, by contrast, are bigger, harder to conceal, less innocuous in appearance if found by a parent or teacher, not ready for immediate use, more complicated to adjust or assemble, require constant refilling with nicotine liquids, and generally cannot be recharged by plugging into a USB port. *See* A.200.

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CDC Visual Dictionary at 10, 12 (cartridge-based vaping pen with USB-rechargeable battery on the left; open tank systems on the right).

FDA said it was important to issue the 2020 Enforcement Guidance because the agency had not previously distinguished between cartridge-based and tank-based e-cigarettes—a distinction it thought important because the former are comparatively more attractive to youth. *See* A.202. FDA's previous enforcement guidance also did not include mint-flavored e-cigarettes as "flavored" products—an omission it thought necessary to correct, again, based on comparative attractiveness to youth. *Ibid.* So FDA provided notice to the regulated industry about its then-current thinking, based on the then-existing data, so everyone was on fair notice that flavored (including mint-flavored) cartridge-based e-cigarettes were particularly attractive to youth users. FDA thus announced that it had "recalibrated its balancing of public health considerations in light of the public health threats and the significant new evidence described above." A.204.

* * *

The dizzying detail in the foregoing introduction has an important point: Never in this long, winding, and byzantine regulatory process of meetings, PowerPoint decks, proposed rules, comment periods, guidance documents, and enforcement priorities did FDA *ever* say that it was contemplating an across-the-board ban on flavored products. It emphasized all sorts of relatively minor distinctions—including whether mint is a flavor, the size difference between vape pens and tanks, and age-access restrictions for online ads. And FDA conspicuously announced when and how—supported by data and reasoned analysis—it "recalibrated" its understanding of public health to focus on nicotine cartridges as opposed to nicotine e-liquids. But at no point did the agency *ever* say that it was contemplating a categorical ban on flavored e-cigarettes.

Nor did FDA ever give fair notice that *flavored* product manufacturers had to submit robust scientific studies on *flavored* ***369** e-cigarette products. To the contrary, the entirety of FDA's pre-decisional guidance was premised on these facts:

- Limited scientific data exists for ENDS products generally (flavored or unflavored). *See* A.298–99, A.317 (June 2019 Guidance).
- Flavored PMTAs could and should include existing data regarding *unflavored* products generally to make inferences about the public health benefits of *flavored* products generally. *See* A.300 (June 2019 Guidance); October 2018 Guidance at 11–17.

- FDA did not expect flavored product manufacturers to conduct new, long-term, scientific studies that directly measured the behaviors of people who use Triton's and Vapetasia's flavored products specifically. A.299, A.317 (June 2019 Guidance).

- And FDA expected that flavored product manufacturers would submit observational studies, which include surveys. A.324 (June 2019 Guidance); *see also* October 2018 Guidance at 16–17 (discussing acceptable consumer perception data without any reference to conducting such surveys over time).

B.

1. Wages and White Lion Investments, LLC, doing business as Triton Distribution and Vapetasia, LLC (collectively "petitioners") manufacture bottles of flavored nicotine *liquids*. Vapers use such nicotine liquids to refill their tank systems and other e-cigarette products. Petitioners do *not* make e-cigarettes, vape pens, vape pods, vape cartridges or any other vaping device covered by the 2020 Enforcement Guidance. Petitioners bottle only the liquid, and hence it is common ground that FDA's 2020 Enforcement Guidance did not apply to petitioners or their liquids.

On September 9, 2020, approximately eight months after FDA issued its 2020 Enforcement Guidance, petitioners timely filed PMTAs for their flavored nicotine liquids. "Triton's bundled PMTA was nine gigabytes in size, consisting of hundreds of individual files, including the marketing and sales-access restriction plans containing the measures described above to limit youth access and use of its products." Petrs' EB Br. 15. Petitioners submitted long-term, controlled, and peer-reviewed studies to show that e-cigarettes generally cause smokers to switch to vaping and thus save lives. *See, e.g.*, A.369–70, A.431. Petitioners also included observational studies in the form of cross-sectional surveys. *See, e.g.*, A.384, A.403, A.407, A.438. But in accordance with FDA's pre-decisional guidance, petitioners did not conduct new scientific studies on their specific flavored PMTA products. And petitioners did point to robust, reliable, and peer-reviewed scientific studies involving *unflavored* products to draw inferences about *flavored* products (including at least one study that reviewed randomized controlled trials and longitudinal cohorts to show the net public health benefits of e-cigarettes). *See, e.g.*, A.369–71 (collecting studies), A.431 (citing, *inter alia*, Riccardo Polosa et al., *The Effect of E-cigarette Aerosol Emissions on Respiratory Health: A Narrative Review*, 13 EXPERT REV. OF RESPIRATORY MED. 899 (2019)).

In accordance with FDA's instructions that manufacturers should focus on measures to restrict youth access, petitioners offered lengthy explanations for their marketing plans:

> Triton's bottled e-liquids are only sold in age-restricted vape and tobacco-specialty shops and through age-restricted online sales to customers who can show they are at least 21 years old. None of Triton or Vapetasia's ENDS products ***370** have been sold in convenience stores or other general retail outlets. Retailers selling the e-liquids must verify photo IDs of anyone who is 27 or younger before entering the establishment, immediately respond to and remedy any violations, actively display signs indicating that the products are not for sale to minors and that minors are not allowed on the premises, and are subject to contractual penalties if they fail to do so. Triton and its customers screen retailers before establishing or renewing distribution agreements and require retailers to develop internal compliance check programs, such as mystery shopper programs.

Petrs' EB Br. 16 (quotation omitted). Petitioners also implemented third-party verification services to ensure only adults could purchase the products online; voluntarily increased the minimum age for customers to 21 before it was legally required; imposed volume limits on purchases; limited labeling to exclude cartoons or childish images or vivid colors; limited online marketing to exclude human models; and limited other marketing to age-restricted channels. *See id.* at 16–18. Petitioners also included a survey to show that more than two-thirds of their customers are over the age of 35. *See id.* at 18.

2. On August 26, 2021, FDA issued a press release to announce the *en masse* denial of 55,000 flavored e-cigarette

applications. *See* FDA, *FDA Denies Marketing Applications for About 55,000 Flavored E-Cigarette Products for Failing to Provide Evidence They Appropriately Protect Public Health* (Aug. 26, 2021), https://perma.cc/LCD8-VWGQ ("August 2021 press release"). In that press release, FDA announced for the first time that, for flavored e-cigarette applications, the agency *would* require "a randomized controlled trial," a "longitudinal cohort study," or some other scientific study that was comparably "robust and reliable." *Ibid.* FDA said nothing to acknowledge that its new requirement for scientific studies conflicted with its previous guidance. Rather, using its new scientific-studies-or-bust standard announced in the press release, FDA denied 946,000 flavored-product applications in just over two weeks. *See* FDA, *FDA Makes Significant Progress in Science-Based Public Health Application for Review, Taking Action on Over 90% of More than 6.5 Million 'Deemed' New Tobacco Products Submitted* (Sept. 9, 2021), https://perma.cc/4F69-MRUB. As of today, FDA has not approved a single PMTA for a single one of the more than 1,000,000 flavored e-cigarette products submitted to the agency.

Immediately after receiving the new scientific-studies-or-bust requirement in the August 2021 press release, petitioners asked FDA for time to perform the newly required studies. Without acknowledging that request, on September 14 and 16, 2021, FDA issued marketing denial orders ("MDOs") to Triton and Vapetasia, finding that their PMTAs failed to include the once-optional-but-now-required scientific studies. Specifically, FDA stated:

> All of your PMTAs lack sufficient evidence demonstrating that your flavored [ENDS] will provide a benefit to adult users that would be adequate to outweigh the risks to youth .... This evidence could have been provided using a randomized controlled trial and/or longitudinal cohort study that demonstrated the benefit of your flavored [ENDS] products over an appropriate comparator tobacco-flavored [ENDS]. Alternatively, FDA would consider other evidence but only if it reliably and robustly evaluated the impact of the new flavored vs. Tobacco-flavored products on adult smokers' switching or cigarette reduction over time.

***371** A.57. FDA also stated that it refused even to read petitioners' marketing plans. *See* A.93 n.xix; A.145 n.xix.

3. Petitioners timely moved to stay their marketing denial orders pending review in our court. A unanimous motions panel granted that motion, concluding that Triton was likely to succeed on the merits. *See Wages & White Lion Invs., LLC v. FDA*, 16 F.4th 1130 (5th Cir. 2021) ("*Stay Op.*"). Subsequently, a divided merits panel nonetheless rejected the petitions for review. *Wages & White Lion Invs., LLC v. FDA*, 41 F.4th 427 (5th Cir. 2022) ("*Panel Op.*"). In dissenting from the panel opinion, Judge Jones described FDA's actions as "a mockery of 'reasoned' administrative decision-making." *Id.* at 442 (Jones, J., dissenting). Specifically, JUDGE JONES explained:

> The majority's analysis of these MDOs looks almost exclusively at the bottom-line result of FDA's decisions and finds nothing to criticize. But the facts recited above speak for themselves. FDA refused to review petitioners' marketing restrictions, which it had repeatedly stated were key to discouraging youthful use of the products and were thus critical components of the PMTAs. FDA repeatedly counselled applicants that long term studies were likely unnecessary and it said nothing about comparative efficacy studies—until the PMTA deadline was long gone; and then it refused petitioners the opportunity to conduct such studies. Finally, FDA's defense against petitioners on the merits of their applications is loaded with post hoc rationalizations. Any of these errors is a "fatal flaw." Taken together, they are mortal wounds.

Id. at 446. We granted rehearing and vacated the panel opinion. 58 F.4th 233 (5th Cir. 2023) (mem.).

II.

The first question is whether FDA acted arbitrarily and capriciously in rejecting petitioners' PMTAs. It did. Four well-established and longstanding principles of administrative law independently require that result: (A) An agency cannot invent *post hoc* justifications for its decision in court and outside the administrative record. (B) An agency must provide fair notice before it deprives a citizen of property. (C) When an agency changes its position, it must display awareness of the change and explain it. And (D) even when an agency acknowledges and explains a change in its position, it cannot fault a regulated entity for relying in good faith on the previous one.

A.

First, the prohibition on *post hoc* rationalizations. This rule is even older than the Administrative Procedure Act of 1946, 5 U.S.C. §§ 551–559 ("APA"). It dates back at least to the first decision in *Chenery*, where the Court said: "The grounds upon which an administrative order must be judged are those upon which the record discloses that its action was based." *SEC v. Chenery Corp.* (*Chenery I*), 318 U.S. 80, 87, 63 S.Ct. 454, 87 L.Ed. 626 (1943). The agency is not free to defend its decision by supplying new, *post hoc* rationalizations for it when sued. *See, e.g., Burlington Truck Lines v. United States*, 371 U.S. 156, 168–69, 83 S.Ct. 239, 9 L.Ed.2d 207 (1962); *Citizens to Pres. Overton Park, Inc. v. Volpe*, 401 U.S. 402, 419, 91 S.Ct. 814, 28 L.Ed.2d 136 (1971); *Am. Textile Mfg. Inst., Inc. v. Donovan*, 452 U.S. 490, 539, 101 S.Ct. 2478, 69 L.Ed.2d 185 (1981); *DHS v. Regents of the Univ. of Cal.*, —— U.S. ——, 140 S. Ct. 1891, 1908–09, 207 L.Ed.2d 353 (2020).

Consider for example the most significant case ever to elucidate the arbitrary-and-capricious ***372** standard: *Motor Vehicle Manufacturers Association of the United States v. State Farm Mutual Auto. Insurance Co.*, 463 U.S. 29, 103 S.Ct. 2856, 77 L.Ed.2d 443 (1983). In that case, the National Highway Traffic Safety Administration ("NHTSA") rescinded its safety regulation for passive restraints (automatic seatbelts and airbags) in cars. *Id.* at 38, 103 S.Ct. 2856. The agency reasoned that automatic seatbelts were ineffective because owners could easily detach them, thus reducing or eliminating the safety benefit. *Id.* at 39, 103 S.Ct. 2856. At no point in the administrative record, however, did the agency even consider the possibility of mandating airbags—much less did the agency explain why an airbag mandate was inadvisable. *Id.* at 48, 103 S.Ct. 2856. When the case entered the courts, the agency tried to provide the missing rationale. Specifically, its appellate counsel pointed to "questions concerning the installation of airbags in small cars" and "adverse public reaction" as reasons for the agency's failure to consider an airbag mandate. *Id.* at 50, 103 S.Ct. 2856. The Supreme Court emphatically rejected that lawyerly effort: "The short—and sufficient—answer to petitioners' submission is that the courts may not accept appellate counsel's *post hoc* rationalizations for agency action. It is well-established that an agency's action must be upheld, if at all, on the basis articulated by the agency itself." *Ibid.* (quotation omitted); *accord, e.g., Int'l Union, United Mine Workers of Am. v. Mine Safety & Health Admin.*, 626 F.3d 84, 94 (D.C. Cir. 2010) (rejecting statements at oral argument as prohibited *post hoc* rationalizations); *Conn. Dep't of Pub. Util. Control v. FERC*, 484 F.3d 558, 560 (D.C. Cir. 2007) (same).

So too here. In its pre-MDO guidance to manufacturers, FDA said that marketing plans were "critical" to the success of e-cigarette applications. PMTA Proposed Rule, 84 Fed. Reg. at 50,581. It told manufacturers to submit their marketing plans in mind-numbing detail—including "sales data broken down by population demographics and tobacco use status"; sales data broken down by Universal Product Code and four-week intervals; sales data broken down "by U.S. census region, major retail markets, and channels in which the product is sold (e.g., convenience stores, food and drug markets, big box retailers, internet/online sales, tobacco specialty shops) [*sic*] promotional discounts (e.g., buy-one-get-one free or percentage discount"; and comparable information for "top selling brands as a comparison" to the manufacturer's product. A.325. FDA also requested information on advertising, marketing strategies, point of sale restrictions, social media restrictions, and many other details. Why? Because all of this information was essential to "enable FDA to better understand the potential consumer demographic." *Ibid.*

In the MDOs, however, FDA explicitly stated that its instructions were all for naught. First, FDA determined that the *mere existence of flavor* was sufficient to justify denial of a PMTA because flavor standing alone was enough to prove that youth would use the proposed product and that youth use would outweigh any countervailing benefit to adults. Gone was any suggestion that a manufacturer could do anything to limit youth access to its products. And second, FDA stated

that it did not even read the marketing plans it previously said were critical: "For the sake of efficiency, the evaluation of the marketing plans in applications will not occur at this stage of review, and *we have not evaluated any marketing plans submitted with these applications.*" A.145 n.xix (emphasis added).

***373** At some point in this litigation, FDA's very able counsel presumably recognized that sentence spelled trouble for the agency. And as the Eleventh Circuit correctly held, FDA's refusal even to read the once-"critical" marketing plans constituted an arbitrary and capricious failure to consider "an important aspect of the problem." *Bidi Vapor LLC v. FDA*, 47 F.4th 1191, 1203 (11th Cir. 2022) (quoting *State Farm*, 463 U.S. at 43, 103 S.Ct. 2856).

So at oral argument before the merits panel in our court, FDA's counsel flatly contradicted the administrative record and stated that FDA did in fact look at "summar[ies]" of petitioners' marketing plans. *Panel Op.*, 41 F.4th at 441. This position cannot conceivably be characterized as "[c]larifying what happened factually." *Id.* at 441 n.17. The administrative record says FDA did "not evaluate[ ] any marketing plans submitted with these applications." A.145 n.xix. At oral argument, FDA's counsel said the opposite. That is barred by the venerable prohibition on *post hoc* justifications that federal courts have consistently applied since at least *Chenery I.*

Moreover, even if we could look past the *post hoc* prohibition, FDA's *post hoc* statements underscore the agency's arbitrariness. For example, in its pre-MDO guidance documents, FDA excluded menthol-flavored e-cigarettes from its definition of "flavored" products. *See, e.g.*, A.186. And presumably because of that exclusion, FDA has approved menthol-flavored e-cigarette products notwithstanding its ban on "flavored" products. The rationale? According to the 2020 Enforcement Guidance, menthol products are less popular with youth than are flavored products. *See, e.g.*, A.198 (collecting survey data and finding "youth use of menthol-flavored products is not as high as that for mint-and fruit-flavored products."). Yet in its en banc brief before the court, FDA makes a *post hoc* invocation of "recent data [that purportedly] demonstrate 'prominent menthol e-cigarette use' among middle-and high-school e-cigarette users." FDA EB Br. 23. And FDA makes no attempt to explain why, if that's true, it approved menthol products. Or more to the point, how it could rationally approve menthol products while denying petitioners' flavored products.

The dissent by JUDGE HAYNES disagrees. JUDGE HAYNES believes "the FDA clarified at oral argument that it *did* review summaries of Petitioners' marketing plans contained within their PMTAs" and that this is the "type of factual clarification we seek at oral argument." *Post*, at 405 (Haynes, J., dissenting). For this proposition, the dissent first cites *Cooper Cameron Corp. v. U.S. Dep't of Lab., OSHA*, 280 F.3d 539, 542 (5th Cir. 2002). Although that case has an agency as a party in the caption, it is not an administrative law case. Nor does it implicate *Chenery I.* The dissenting opinion cannot point to a single case where we allowed an administrative agency to defend its action by countermanding an express statement in the administrative record. *Cf. Schofield v. Saul*, 950 F.3d 315, 322 (5th Cir. 2020) (holding an agency can waive an argument in its favor but saying nothing about an agency's ability to countermand its record statements). Or any authority that allows agencies to rehabilitate deficiencies in the administrative record solely by answering friendly questions at oral argument.

We instead underscore our agreement with JUDGE GRAVES on this point:

> [T]his court may, and often does, seek clarification at oral argument. But the FDA's statement does not clarify. Among other things, the statement raises the question of why, if the FDA did review the summaries, it told Petitioners that it had "not evaluated any marketing ***374** plans." As it stands, the FDA's statement at oral argument is at odds with the record. For that reason alone, the court should disregard it.

Post, at 406 (Graves, J., dissenting).

B.

Second, the fair notice doctrine. It is common ground between the parties that the fair notice doctrine applies. Petitioners repeatedly invoked it at the stay stage, before the panel, and in their en banc brief. And FDA has never disputed its applicability. FDA's only contention is that it satisfied the

doctrine when it "gave fair notice of the analysis the agency would perform" in adjudicating e-cigarette applications. FDA EB Br. 37 (quotation omitted). We therefore (1) begin with the fair notice doctrine and then (2) explain FDA's violation of it. Finally, we (3) reject FDA's attempts to find fair notice in the pre-decisional guidance documents that omitted it.

1.

The fair notice doctrine is a well-established principle of administrative law. *See* *Rollins Env't Servs. (NJ) Inc. v. EPA*, 937 F.2d 649, 654 n.1, 655 (D.C. Cir. 1991) (Edwards, J., concurring in part and dissenting in part) (fair notice doctrine is "basic hornbook law in the administrative context" and a "simple principle of administrative law"). At its core, the doctrine requires administrative agencies to give the public fair notice of their rules before finding a violation of them. As we explained the doctrine in one of the canonical fair notice cases:

> The respondents contend that the regulations should be liberally construed to give broad coverage because of the intent of Congress to provide safe and healthful working conditions for employees. An employer, however, is entitled to fair notice in dealing with his government. Like other statutes and regulations which allow monetary penalties against those who violate them, an occupational safety and health standard must give an employer fair warning of the conduct it prohibits or requires ....
>
> If a violation of a regulation subjects private parties to criminal or civil sanctions, a regulation cannot be construed to mean what an agency intended but did not adequately express .... [T]he Secretary as enforcer of the Act has the responsibility to state with ascertainable certainty what is meant by the standards he has promulgated.

Diamond Roofing Co. v. Occupational Safety & Health Rev. Comm'n, 528 F.2d 645, 649 (5th Cir. 1976); *see also* *Gates & Fox Co. v. Occupational Safety & Health Rev. Comm'n*, 790 F.2d 154, 156 (D.C. Cir. 1986) (relying on *Diamond Roofing* to formulate the D.C. Circuit's fair notice doctrine).

The fair notice doctrine is rooted in the Fifth Amendment's Due Process Clause. *Gen. Elec. Co. v. EPA*, 53 F.3d 1324, 1328–29 (D.C. Cir. 1995); *see also* *United States v. Chrysler Corp.*, 158 F.3d 1350, 1354–55 (D.C. Cir. 1998); Albert C. Lin, *Refining Fair Notice Doctrine: What Notice is Required of Civil Regulations*, 55 BAYLOR L. REV. 991, 992–98 (2003). Obviously, the Fifth Amendment is traditionally relevant to criminal proceedings. *See* *Gates & Fox*, 790 F.2d at 156. And in the criminal context, fair notice requirements are well understood. As Justice Holmes explained in overturning a criminal conviction, "a fair warning should be given to the world in language that the common world will understand, of what the law intends to do if a certain line is passed." *McBoyle v. United States*, 283 U.S. 25, 27, 51 S.Ct. 340, 75 L.Ed. 816 (1931).

***375** But the fair notice doctrine also applies more broadly to civil administrative proceedings:

> [A]s long ago as 1968, we recognized this "fair notice" requirement in the civil administrative context. In *Radio Athens, Inc. v. FCC*, we held that when sanctions are drastic—in that case, the FCC dismissed the petitioner's application for a radio station license—"elementary fairness compels clarity" in the statements and regulations setting forth the actions with which the agency expects the public to comply.

Gen. Elec. Co., 53 F.3d at 1329 (quoting *Radio Athens, Inc. v. FCC*, 401 F.2d 398, 404 (D.C. Cir. 1968)); *see also* *ibid.* (emphasizing fair notice doctrine "has now been thoroughly 'incorporated into administrative law,' " far outside criminal proceedings (quoting *Satellite Broad. Co. v. FCC*, 824 F.2d 1, 3 (D.C. Cir. 1987))). For example, the D.C. Circuit applied the doctrine to a product recall in *Chrysler*. 158 F.3d at 1351, 1354–55. The D.C. Circuit applied the doctrine to a $25,000 fine in *General Electric*. 53 F.3d at 1327, 1329–30. And, most relevant to the present controversy, the D.C. Circuit has repeatedly applied the doctrine to the "drastic" sanction of denying applications for radio and cellular licenses in cases like *Radio Athens*, 401 F.2d at 400, 404, *Satellite Broadcasting*, 824 F.2d at 2–4, and *McElroy Elecs. Corp. v. FCC*, 990 F.2d 1351, 1353, 1363 (D.C. Cir. 1993). If there is a "drasticness" distinction between the denial of a cellular license application and the denial of a tobacco marketing application, FDA does not point to it. And it is hard to imagine one, given the MDOs in this case will unquestionably put petitioners out of business. *See* EB Oral Arg. at 13:07–49. So we take it as undisputed that the fair notice doctrine applies.

Chrysler provides a helpful illustration of the doctrinal contours of the fair notice requirement. In that case, NHTSA promulgated a seatbelt safety standard called "Standard 210." *See Chrysler*, 158 F.3d at 1351. Standard 210 required carmakers to install seatbelt anchorages that could withstand certain pressure forces for certain durations of time. *Ibid.* The standard further required carmakers to conduct their pressure tests using a "pelvic body block," an L-shaped metal block resembling a human pelvis. *Ibid.* Standard 210 did not specify, however, *where* carmakers should install the pelvic body blocks in their tests. *Ibid.* (citation omitted). So Chrysler put the pelvic block against the seat back—a reasonable decision given how people sit in cars and given that "NHTSA's own test schematic for Standard 210, entitled 'Typical FMVSS 210 Anchorage Pull Test Setup,' shows the pelvic body block against the seat back." *Id.* at 1356. On those parameters, Chrysler's cars met Standard 210. *Ibid.*

NHTSA nonetheless required Chrysler to recall 91,000 cars. *Id.* at 1351. NHTSA pointed out that nothing in Standard 210 *guaranteed* that a car would pass the testing pressures when the pelvic block was pressed against the seat back. *Id.* at 1355–56. To the contrary, the Standard itself did not specify a location for the block. *Id.* at 1356. And the agency put the world on notice that when a Standard is silent about testing locations, the carmaker must be able to meet the testing pressures at any and all testing locations. Specifically, the agency published this notice in the Federal Register:

> As a general matter, when a standard does not specify a particular test condition, there is a presumption that the requirements of the standard must be met at all such test conditions. This presumption that the standard must be met at all positions of unspecified test conditions ***376** may be rebutted if the language of the standard as a whole or its purposes indicate an intention to limit unspecified test conditions to a particular condition or conditions.
>
> In the case of the strength requirements in Standard No. 210, nothing in the language of the standard suggests that the strength requirements were only to be measured with the safety belt or other vehicle features at certain adjustment positions. Indeed, the purpose of the standard is to reduce the likelihood that an anchorage will fail in a crash. To serve this purpose, the anchorage must be capable of meeting the strength requirements with the safety belt and other vehicle features at any adjustment, since those features could be at any adjustment position during a crash.

Federal Motor Vehicle Safety Standards; Seat Belt Assembly Anchorages, 56 Fed. Reg. 63,676, 63,677 (1991). And when the pelvic block was moved *away* from the seat back, the seatbelt anchors failed the pressure test. *Chrysler*, 158 F.3d at 1352. NHTSA argued that the plain language of the Federal Register put Chrysler on fair notice of its testing obligations and required recall of the unsafe cars. *Id.* at 1356. After Chrysler refused to institute a recall, NHTSA sued the carmaker. *Id.* at 1352.

Chrysler won. Even though the Federal Register told Chrysler that it needed to satisfy Standard 210 "at *all positions* of unspecified test conditions," 56 Fed. Reg. at 63,677 (emphasis added), the D.C. Circuit held this language was "far too general" to give Chrysler fair notice of its obligations to move the pelvic block. *Chrysler*, 158 F.3d at 1356. It also did not matter that NHTSA previously told regulated entities not to rely on the testing schematic attached to Standard 210 because "an agency is hard pressed to show fair notice when the agency itself has taken action in the past that conflicts with its current interpretation of a regulation." *Ibid.* (citing *Gen. Elec. Co.*, 53 F.2d at 1332). In sum, "Chrysler might have satisfied NHTSA with the exercise of extraordinary intuition or with the aid of a psychic, but these possibilities are more than the law requires." *Id.* at 1357.

2.

So too here. The differences between the October 2018 Guidance and the June 2019 Guidance on the one hand and FDA's across-the-board denials of every flavored PMTA on the other are far starker than in *Chrysler.*

Guidance: In the October 2018 Guidance, FDA told petitioners: "*No specific studies are required for a PMTA*; it may be possible to support a marketing order for an ENDS product without conducting new nonclinical or clinical studies given other data sources can support the PMTA." October 2018 Guidance at 26 (emphasis added). It also told petitioners: "Youth behavioral data **not** required at this time." *Id.* at 18 (emphasis in original). And it never told petitioners they could not rely on existing data from *unflavored* products to support their *flavored* PMTAs. To the contrary, in the June 2019 Guidance, FDA *twice* told petitioners: "[I]n general, *FDA does not expect that applicants will need to conduct long-term studies to support an application.*" A.299 (emphasis added); *see also* A.317 (same). FDA instead

invited flavored manufacturers to rely on existing data (including studies of smokers and users of unflavored ENDS products) to make inferences about flavored ENDS products. October 2018 Guidance at 11–12. And both the June 2019 Guidance and the October 2018 Guidance invited petitioners to use "observational studies," which could include surveys. ***377** A.324 (June 2019 Guidance); *see also* October 2018 Guidance at 16–17.

MDOs: Then FDA flip-flopped. FDA turned around and denied petitioners' applications because they did not perform "a randomized controlled trial and/or longitudinal cohort study" or other comparably robust evidence that directly measured the behaviors of those who use their flavored products. *See* A.57, A.85 & n.vi. And when petitioners submitted voluminous, robust scientific studies to show e-cigarettes induce adults to switch from smoking (and thus save lives), FDA categorically rejected that data as irrelevant because it did not show *flavored* e-cigarettes promote more switching than *unflavored* ones. *See* A.57. And FDA ignored as irrelevant petitioners' observational cross-section studies without any acknowledgement that the agency previously invited them.

3.

FDA's principal justification for its about-face is that it provided manufacturers fair notice of the PMTA requirements in the June 2019 Guidance. *See* FDA EB Br. 29–37. Specifically, FDA points to one sentence in that 52-page, single-spaced guidance document: "We recommend an applicant compare the health risks of its product to both products within the same category and subcategory, as well as products in different categories as appropriate." A.299; *see also* FDA EB Br. 36 (relying on this sentence alone to provide fair notice). But it is undisputed that petitioners compared the health risks of their products to other products in the same or different categories. As FDA itself concedes in its en banc brief:

> Petitioners asserted in their application that "flavors are crucial to getting adult smokers to make the switch and stay away from combustible cigarettes," A379; that adult smokers prefer flavored e-cigarettes to tobacco-flavored e-cigarettes, A380; and that this preference "has powerful implications for not only the role of flavors in helping smokers' transition from smoking to vaping, but also in connection with helping vapers maintain smoking abstinence and preventing relapse to smoking," *id.*

FDA EB Br. 35. Thus, there is no question that petitioners compared the health risks of their products to other products as the June 2019 Guidance recommended.

The question is whether FDA gave petitioners fair notice of their need to provide *long-term scientific studies as proof* of those relative risks. And on that question, the very best sentence FDA can find is this one from its June 2019 Guidance: "Nonclinical studies alone are generally not sufficient to support a determination that permitting the marketing of a tobacco product would be appropriate for the protection of the public health." A.298. From that, FDA argues that it gave petitioners fair notice that they might be obligated to conduct new long-term scientific studies on their flavored products. FDA EB Br. 31. Of course, saying *X* might not be sufficient is a far cry from saying *Y* is necessary. But more fundamentally, the agency's position beggars belief because it ignores *the very next sentence* in the guidance document: "[I]n general, FDA does not expect that applicants will need to conduct long-term studies to support an application." A.299. FDA also ignores that the very same paragraph says "FDA understands that limited data may exist from scientific studies and analyses" to support e-cigarette applications. A.298. And FDA ignores that the very same guidance document comes back to this point a few pages later:

> Due to the emerging nature of ENDS products within the general tobacco market, FDA acknowledges that there may be limited nonclinical or clinical research ***378** conducted on specific ENDS products. Thus, it is likely that applicants will conduct certain investigations themselves and submit their own research findings as a part of their PMTA. *However, in general, FDA does not expect that applicants will have to conduct long-term studies to support an application.*

A.317 (emphasis added). The agency simply cannot contend that when it twice said "FDA does not expect that applicants will have to conduct long-term studies to support an application" for a specific flavored product, A.299, A.317,

it put petitioners on fair notice that "FDA will deny your application if you do not conduct long-term studies on your specific flavored product."

Nor can FDA deny that it in fact required long-term studies. In its explanation for denying petitioners' applications, FDA imposed two requirements—randomized controlled trials and longitudinal cohort studies. Then it found both of those long-term scientific studies lacking in petitioners' applications, for the obvious reason that FDA previously said these studies were unnecessary:

Presence of Evidence for Flavored ENDS Products

Criterion A	Present		Absent
Randomized Controlled Trial (RCT) on new product use and smoking behavior	☐		☒
Instructions: To select "Present", all of the following boxes must be checked "Yes":	Yes	No	N/A[2]
Was the RCT conducted using new products?	☐	☐	☒
Does the RCT include a tobacco-flavored arm and a flavored product arm[3]?	☐	☐	☒
Do the outcomes include users' ENDS and smoking behavior to assess switching and/or cigarette reduction (e.g., measures of cigarettes per day, smoking cessation, ENDS use)?	☐	☐	☒
Comment(s): N/A			

Criterion B	Present		Absent
Longitudinal Cohort Study (LCS) on new product use and smoking behavior	☐		☒
Instructions: To select "Present", all of the following boxes must be checked "Yes":	Yes	No	N/A[2]
Was the LCS conducted and does it include users of new products who are followed over time?	☐	☐	☒
Was use of tobacco-flavored products and other flavored products assessed[3]?	☐	☐	☒
Do outcomes include users' ENDS and smoking behavior to assess switching and/or cigarette reduction (e.g., measures of cigarettes per day, smoking cessation, ENDS use)?	☐	☐	☒
Comment(s): N/A			

A.70. That sure looks like a requirement that petitioners perform long-term scientific studies on their e-cigarette products; otherwise, it is hard to understand why FDA would devote the overwhelming majority of its decision document to rejecting the PMTAs for failing to include such studies. True, FDA then included a single sentence regarding "other" scientific evidence:

***379**

Criterion C
Other evidence in the PTMA(s) related to potential benefit to adults None

A.71 (Triton); *see also* A.134 (similar one-sentence rejection for Vapetasia). But FDA made clear it could be persuaded by "other evidence" "*only* if it reliably and robustly evaluated the impact of the new flavored vs. Tobacco-flavored products on adult smokers' switching or cigarette reduction *over time.*" A.57 (emphasis added).

To the extent that "reliably and robustly" evaluating impact "over time" means a randomized controlled trial or a longitudinal cohort study, that is obviously a violation of the fair notice doctrine for the reasons explained above. FDA cannot require petitioners to perform such long-term/over-time studies after telling petitioners that, "[d]ue to the emerging nature of ENDS products within the general tobacco market, FDA acknowledges that there may be limited nonclinical or clinical research conducted on specific ENDS products." A.317; *see also* A.298 (same). Yet in its "technical project lead" supporting the MDOs, FDA said this about the "other evidence" it would consider "on a case-by-case basis":

> For example, we would consider evidence from another study design if it could *reliably and robustly* assess *behavior change* (product switching or cigarette reduction) *over time, comparing users* of flavored products with those of tobacco-flavored products. In our review of PMTAs for flavored ENDS so far, we have learned that, *in the absence of strong evidence generated by directly observing the behavioral impacts* of using a flavored product vs. a tobacco-flavored product *over time*, we are unable to reach a conclusion that the benefit outweighs the clear risks to youth.

A.85 n.vi (emphases added). Again, that looks like a requirement for direct observations and controlled scientific studies, supported by strong and robust statistical evidence, which FDA previously said it did not require.

If "reliably and robustly" evaluating impact "over time" instead means something else, petitioners (and the courts) are left simply to imagine what the agency might have had in mind. FDA and the dissenting opinions do not say what "other evidence" petitioners might have supplied to win approval. Instead, one of the dissenting opinions disputes the premise that an agency must specify the grounds for its decisions because, as the dissenting opinion puts it, "the FDA must use its science to evaluate the applications." *Post*, at 394 (Haynes, J., dissenting). It is obviously true that science matters—and it is also true that agencies must give regulated entities fair

notice of *what* science matters. If an agency could instead move the scientific goalposts and then refuse to specify the new scientific goal line, the administrative process would be governed not by science but by diktat.

And it is flatly untrue that petitioners' "other evidence" was "None." A.71 (Triton); *see also* A.134 (Vapetasia's MDO, stamping its "other evidence" as "N/A"). Rather, it is undisputed that petitioners *did* present *some* "other evidence." For example, Triton submitted:

> ***380** published studies and articles, as well as subject matter databases, related to the topic areas identified in FDA's PMTA Guidance: in vivo and in vitro toxicology (e.g., carcinogenesis, genotoxicity, mutagenicity, reactive oxygen species, inflammation, cytotoxicity, respiratory health, cardiovascular disease, and reproductive and developmental toxicity), clinical health, abuse liability and pharmacokinetics, trends in usage and factors that influence ENDS usage (e.g., susceptibility, consumer perception, initiation, cessation, transition), topography, human factors, biomarkers of harm and exposure, and population health (e.g., FDA's Population Assessment of Tobacco and Health (PATH)).

A.369–70. Triton also pointed to peer-reviewed studies, long-term randomized controlled studies, longitudinal cohort studies, short-term studies, and a meta-analysis by the National Academies of Science, Engineering, and Medicine to show the public health benefits of e-cigarette use by cigarette smokers. *See, e.g.*, A.431. The dissenting opinions do not explain why or how this science could be rejected out of hand with FDA's one-word rubber stamp labeled "None" or "N/A."

FDA, by contrast, *did* explain why the PMTAs could be summarily rejected for submitting "None" of the studies FDA belatedly demanded: It created a new, after-the-fact, categorical ban on using scientific data from *unflavored* products to support *flavored* PMTAs. In its MDOs, the agency said petitioners should have submitted scientific studies on the public health benefits of *their specific, flavored* e-cigarette liquids: As FDA put it, petitioners should have submitted "a randomized controlled trial and/or longitudinal cohort study that demonstrated the benefit of *your* flavored [ENDS] products over an appropriate comparator tobacco-flavored [ENDS]." A.57 (emphasis added). Or petitioners should have submitted some unspecified "other evidence" that "reliably and robustly evaluated" the public health benefits of *petitioners' specific* "new flavored" products. *Ibid.* This new approach—adopted for the first time in the MDOs and after years of contrary guidance—prohibited *flavored* product manufacturers from relying on existing data involving *unflavored* products.

The problem of course is that FDA never gave petitioners fair notice that they needed to conduct long-term studies on their specific flavored products. And crucially, FDA never told petitioners that their "other evidence" categorically could not include existing studies involving *unflavored* e-cigarettes. To the contrary, the entirety of FDA's voluminous pre-decisional guidance said the precise opposite: "Due to the emerging nature of ENDS products within the general tobacco market, FDA acknowledges that there may be limited nonclinical or clinical research conducted on specific ENDS products." A.317; *see also* A.298 (same). And FDA told petitioners they did *not* need to conduct long-term studies on their specific products. *See* A.299, A.317. To the contrary, FDA promulgated detailed instructions on how petitioners could build a "bridge" from existing studies[4] to support their PMTAs. *See,* ***381** *e.g.*, A.332–36. Then FDA turned around and categorically banned flavored-product manufacturers from relying on any study that did not focus on the specific flavored product mentioned in the PMTA. Petitioners "might have satisfied [FDA] with the exercise of extraordinary intuition or with the aid of a psychic, but these possibilities are more than the law requires." *Cf. Chrysler*, 158 F.3d at 1357. That warrants vacatur of the MDOs and remand to the agency for a lawful consideration of petitioners' applications.

4 The caveats FDA placed on "bridging" further underscore the capriciousness of its flip-flop in the MDOs. For example, in its pre-decisional guidance, FDA told e-cigarette manufacturers how they could "bridge" from existing literature reviews:
[W]hen you submit a literature review to support an ENDS PMTA, FDA recommends that you consider

the relevancy of the literature and adequacy of the study design in order to determine the likelihood that a particular body of literature will support a marketing order for the new tobacco product. For example, the following questions may be considered:

• Is the tobacco product in the literature comparable in terms of technology to the new tobacco product?

• Are there data (e.g., range of possible use, emissions under conditions of use, biomarkers of exposure) that can be used to adequately demonstrate comparability?

• Was the product in the literature used in a population that adequately represents the target population for the new tobacco product?

• Is the information in the literature sufficient to determine how the tobacco product was used?

A.334. At no point in that list of caveats did FDA even hint at what it later announced in the MDOs —that literature reviews involving *non-flavored* products are somehow categorically irrelevant to the public health benefits of *flavored* e-cigarettes.

C.

The third hoary principle of administrative law at issue in this case is the change-in-position doctrine. The APA "demand[s] that [the agency] display awareness that it *is* changing position. An agency may not, for example, depart from a prior policy *sub silentio* or simply disregard rules that are still on the books." *FCC v. Fox Television Stations, Inc.*, 556 U.S. 502, 515, 129 S.Ct. 1800, 173 L.Ed.2d 738 (2009) (emphasis in original). Rather, an agency *must* provide a "detailed justification" for its change when "its new policy rests upon factual findings that contradict those which underlay its prior policy; or when its prior policy has engendered serious reliance interests that must be taken into account. It would be arbitrary or capricious to ignore such matters." *Ibid.* (citation omitted).

We (1) explain the change-in-position doctrine and then (2) analyze FDA's violation of it.

1.

The change-in-position doctrine requires careful comparison of the agency's statements at *T0* and *T1*. An agency cannot shift its understanding of the law between those two times, deny or downplay the shift, and escape vacatur under the APA. As the D.C. Circuit put it in the canonical case: "[A]n agency changing its course must supply a reasoned analysis indicating that prior policies and standards are being deliberately changed, not casually ignored, and if an agency glosses over or swerves from prior precedents without discussion it may cross the line from the tolerably terse to the intolerably mute." *Greater Bos. Television Corp. v. FCC*, 444 F.2d 841, 852 (D.C. Cir. 1970) (footnote omitted); *accord Encino Motorcars, LLC v. Navarro*, 579 U.S. 211, 222, 136 S.Ct. 2117, 195 L.Ed.2d 382 (2016) ("When an agency changes its existing position, it ... must at least display awareness that it is changing position and show that there are good reasons for the new policy." (quotation and citation omitted)).

Take for example *Physicians for Social Responsibility v. Wheeler*, 956 F.3d 634 (D.C. Cir. 2020) ("*PSR*"). In that case, the Environmental Protection Agency had a "general[ ]" policy of allowing EPA grant recipients to serve on EPA advisory committees. ***382** *Id.* at 641. The source of that "general" policy was unclear; the D.C. Circuit established it by pointing only to a 2013 Office of the Inspector General report for the proposition that receiving an EPA grant "generally" did not create a financial conflict sufficient to disqualify the recipient from serving on an advisory committee. *See ibid.* (citing OFFICE OF THE INSPECTOR GENERAL, EPA, EPA CAN BETTER DOCUMENT RESOLUTION OF ETHICS AND PARTIALITY CONCERNS IN MANAGING CLEAN AIR FEDERAL ADVISORY COMMITTEES 9–10 (2013) https://perma.cc/8EES-WTNV ("2013 OIG Report")). The underlying OIG report was couched in all of the cautious language so often used for guidance documents drafted inside the Beltway. It purported to provide only "guidance." 2013 OIG Report at 10. It hedged that "[t]his report presents the opinion of the OIG and does not necessarily represent the final EPA position." *Id.* at cover page. And at no point did the 2013 OIG Report *ever promise* that grant recipients could serve on EPA advisory committees. To the contrary, the report *twice* cautioned that grants "could ... potentially present an independence concern," so EPA required committee members to fill out reports and subjected them to thorough independence reviews to identify potential conflicts. *Id.* at 10; *see also ibid.* (separately emphasizing a committee member's "research or grant is a potential area of concern" in certain circumstances).

However flexible, qualified, and hazy the preexisting "guidance" was, EPA changed it in October 2017. In that month, the then-new EPA administrator issued a "directive." *PSR*, 956 F.3d at 641. In that 2017 directive, the EPA administrator found it would "strengthen and improve the independence, diversity, and breadth of participation on EPA federal advisory committees" to disqualify EPA grant recipients from participation. *Ibid.* Several grant recipients who wanted to keep their committee assignments claimed EPA violated the APA in changing its pre-2017 guidance.

The D.C. Circuit agreed with the petitioners. The 2017 directive used words like "strengthen" and "improve"—which obviously connote change from the previous standards that needed strengthening and improving. And EPA conceded that the whole purpose of the directive was to change the agency's previous conflicts policy. *See* Brief for EPA at 42–43, *PSR*, 956 F.3d 634 (No. 19-5104), 2019 WL 6895452. ("Anyone reading the Directive and accompanying memorandum would understand that it was being issued precisely because EPA was marking a policy change."). Still, the D.C. Circuit held the agency was not *explicit enough* in announcing to the world that it was changing positions and that its directive was therefore tantamount to a sub silentio policy change. *PSR*, 956 F.3d at 645 (holding EPA said "not a peep" about its pre-2017 conflicts policy). The court of appeals held the change-in-position doctrine required EPA both to explicitly acknowledge the old policy and explain why its new one was better. *Id.* at 647–48. And it mattered not one bit that the previous policy was couched in cautious qualifiers as non-binding "guidance" from the Inspector General. It also did not matter that EPA's directive comported with every applicable substantive law on ethics, conflicts, and advisory committees. Nor did it matter that EPA thought a more robust conflicts policy would serve the public interest. What mattered, the D.C. Circuit held, is that EPA did not acknowledge the 2013 OIG Report and explain its reasons for changing positions. *Ibid.*

Or consider *Southwest Airlines Co. v. FERC*, 926 F.3d 851 (D.C. Cir. 2019). That case involved even more flexible agency policies and standards. FERC had a "general[ ]" policy of relying on two prior-year ***383** inflation data to determine whether an oil pipeline's rate increase was "substantially" too high. *HollyFrontier Refin. & Mktg. LLC v. SFPP, LP*, 162 FERC ¶ 61,232, para. 16 (Mar. 15, 2018). When FERC deviated from that policy to reject Southwest's challenge to a pipeline's rate increase, FERC noted that it never promised to apply the same two-year-data approach to every rate challenge. To the contrary, the Commission emphasized, its heavily qualified standards—replete with cautionary language like "generally" and "substantially"—gave it "considerable discretion" to take a different approach where the facts and the agency's expertise warranted it. Brief for FERC at 17, *Southwest Airlines*, 926 F.3d 851 (No. 18-1134), 2019 WL 1043117. FERC further emphasized that its approach in Southwest's case—to consider more recent data that more accurately reflected the economic reality of the challenged pipeline rate—was unquestionably more accurate than petitioners' contrary approach. *Id.* at 22.

The D.C. Circuit granted the petition for review anyway. True, FERC never *promised* to use any particular cost index. *Southwest Airlines*, 926 F.3d at 858. And true, FERC's approach had the virtue of using the "best available information," which unquestionably served the public interest and best fulfilled the commission's statutory obligations. *Id.* at 856. But none of that mattered because the fundamental fact remained: FERC previously used one cost index, and then it turned around and used a different one without acknowledging the change. *Id.* at 858–59.

2.

Again, so too here. The differences in FDA's positions between the October 2018 Guidance and the June 2019 Guidance on the one hand and the MDOs on the other are radically starker than the difference between EPA's positions in *PSR*. The pre-MDO guidance documents said: "No specific studies are required for a PMTA." October 2018 Guidance at 26. The pre-MDO guidance also said: "[I]n general, FDA does not expect that applicants will need to conduct long-term studies to support an application." A.299; *see also* A.317 (same). If an agency is arbitrary and capricious when it (1) acknowledges changing its position from (2) a policy reflected in a solitary OIG report, *see PSR*, 956 F.3d at 645–48, how much more arbitrary and capricious is the agency when it (1) refuses to acknowledge the change in its position from (2) its own voluminous guidance documents, PowerPoint decks, and enforcement memoranda promulgated over years and reiterated in numerous different ways? Indeed, the *PSR* court even required EPA to explain its change from the position of a *different government agency* (the Office of Government Ethics). *Id.* at 646–47. This is an *a fortiori* case.

Nor can FDA deny that it changed its position based on the qualified language in its pre-MDO guidance documents. It is

unquestionably true that the pre-MDO guidance documents had all manner of disclaimers, qualifiers, and cautionary language. Those documents had headings like "***Contains Nonbinding Recommendations***." A.299; A.317. And FDA never promised or committed itself to doing any particular thing on any particular application. But precisely the same thing was true in *PSR* and *Southwest Airlines*. In *PSR*, the "guidance" was even more cautionary—it wasn't even issued by EPA but instead was issued by the Inspector General, and it contained similar "guidance" disclaimers. And in *Southwest Airlines*, all agreed that FERC never promised to use any particular cost index in adjudicating ***384** Southwest's claims. But that does not matter for purposes of the change-in-position doctrine. In all three cases—*PSR*, *Southwest Airlines*, and this one—the agency violated that doctrine by changing its position without acknowledging the change, and it cannot avoid judicial review by pointing to cautionary headers and words like "generally." *See, e.g.*, *Southwest Airlines*, 926 F.3d at 858.

Nor can FDA deny that it changed its position on cartridge-versus-open systems. In its 2020 Enforcement Guidance, FDA found a material distinction between cartridge-based flavored products and other products, like the e-liquids made by petitioners, that generally refill open-tank systems. *See* A.201–04. Then in its August 2021 press release and its MDOs, FDA imposed an across-the-board ban on *all* flavored products, regardless of device type. As in *PSR* and *Southwest Airlines*, it might very well be true that the agency has the power to impose the policy it wants to impose. And it might very well be true that FDA's ban better serves the public health. But again, that does not matter under the change-in-position doctrine. All that matters here is that the agency unquestionably changed its position and then pretended otherwise. [5]

5 FDA's categorical ban has other statutory problems. For example, the TCA states that FDA must follow notice-and-comment procedures before adopting a "tobacco product standard." *See*21 U.S.C. § 387g(c)–(d). And Congress specifically called a ban on tobacco flavors a "tobacco product standard." *See id.* § 387g(a)(1)(A) (referring to tobacco flavors, "including strawberry, grape, orange, clove, cinnamon, pineapple, vanilla, coconut, licorice, cocoa, chocolate, cherry, or coffee, that is a characterizing flavor of the tobacco product or tobacco smoke"); *see also id.* § 387g(a)(2) (cross-referencing notice-and-comment obligation to revise flavor standards). FDA unquestionably failed to follow § 387g's notice-and-comment obligations before imposing its de facto ban on flavored e-cigarettes.

Were there any doubt on this score, although we think there is none, it would be resolved by the 2020 Enforcement Guidance. In that document, FDA acknowledged all manner of relatively minor changes in its understanding of the public health standard. For example, it went to great lengths to differentiate e-cigarette cartridges from tanks, and to discuss whether "mint" is a flavor. And FDA did so, it acknowledged, because those distinctions reflected changes in the agency's position. *See* A.204. Not only does that prove that FDA understood its obligations to acknowledge such changes, but it also put the public on notice of what it should expect from FDA when and if the agency changed its position. Reasonable manufacturers in petitioners' shoes could expect FDA to continue updating its approach to flavored e-cigarette products. But no reasonable manufacturer could read the 2020 Enforcement Guidance and think the agency would publicly disclose picayune distinctions like whether mint is a flavor while silently requiring the long-term studies it previously said were unnecessary.

FDA failed to acknowledge its multiple changes in position between the pre-MDO guidance documents and the MDOs. That too warrants vacatur of the agency actions and remand for further proceedings. *See, e.g.*, *Southwest Airlines*, 926 F.3d at 859.

D.

The fourth and final deeply rooted administrative law principle at issue in this case is the good faith reliance doctrine. Under it, even when an agency lawfully changes its position, it cannot fault a party for relying in good faith on the prior one. *See, e.g.*, *Christopher v. SmithKline Beecham Corp.*, 567 U.S. 142, 156–57, 132 S.Ct. 2156, 183 L.Ed.2d 153 (2012) (prohibiting agency from penalizing party for "good-faith ***385** reliance" on the agency's prior positions (citation omitted)); *Fox*, 556 U.S. at 515, 129 S.Ct. 1800 (requiring agency to consider "serious reliance interests").

Consider for example *Satellite Broadcasting*. The dispute in that case centered on whether petitioner timely filed an application for a microwave radio license by tendering it to FCC's office in Washington, D.C. *Satellite Broad.*, 824 F.2d at 2. FCC's regulations were ambiguous about where

such applications should be filed. One could reasonably read them to require timely filing in Washington. *Ibid.* Or one could reasonably read them to require timely filing only in Gettysburg, Pennsylvania. FCC chose the former reading, rejected petitioner's latter reading, and rejected the applications as untimely. *Ibid.*

The D.C. Circuit agreed with Satellite Broadcasting, reversed the commission's ruling, and remanded. The court of appeals reasoned the FCC's documents could be reasonably interpreted to require either result. *See id.* at 3 & n.4. But it was precisely because the petitioner could reasonably understand that its actions were permissible that the agency could not ignore that reasonable reliance, reach a contrary result, and reject the applications:

> The Commission through its regulatory power cannot, in effect, punish a member of the regulated class for reasonably interpreting Commission rules. Otherwise the practice of administrative law would come to resemble "Russian Roulette." The agency's interpretation is entitled to deference, but if it wishes to use that interpretation to cut off a party's right, it must give full notice of its interpretation. We accordingly vacate as arbitrary and capricious the FCC's order dismissing these applications and remand this case for their reinstatement *nunc pro tunc.*

Id. at 3–4 (footnote omitted).

Yet again, so too here. Even if we agreed with our sister circuits' decisions that FDA's pre-MDO guidance documents could be reasonably read to put manufacturers on notice of their obligations to perform long-term scientific studies, [6] those documents certainly could be read in good faith the way petitioners read them. There is ample language spread out across multiple documents, multiple PowerPoint decks, and multiple public meetings to say "[n]o specific studies are required for a PMTA"; "[y]outh behavioral data [is] not required at this time"; and manufacturers need not "conduct long-term studies to support an application." *See* October 2018 Guidance at 18, 26; A.299; A.317. There is not a single sentence anywhere in the voluminous record before us that says: "manufacturers should submit long-term scientific studies on the differences between their new flavored e-cigarette products and other non-flavored e-cigarette products." And even if (counterfactually) the agency gave conflicting instructions—"you need not submit long-term studies" and "you should submit long-term studies"—the regulated entity cannot have its application denied because it chose one or the other. *See Satellite Broad.*, 824 F.2d at 4. It follows *a fortiori* that when the agency says: "you need not submit long-term studies" and "this is general guidance," the regulated entity cannot have its application denied because it did not submit long-term studies. To hold otherwise is to turn "the practice of administrative law [into] 'Russian Roulette,' " *ibid.*—where the regulated entity chooses to trust the agency's affirmative statement ("you need not submit long-term studies") ***386** and simply hopes the administrative gun ("this is general guidance") has no bullet in the chamber.

6 *See, e.g., Prohibition Juice Co. v. FDA*, 45 F.4th 8, 22–23 (D.C. Cir. 2022); *Avail Vapor, LLC v. FDA*, 55 F.4th 409, 423 (4th Cir. 2022); *Liquid Labs LLC v. FDA*, 52 F.4th 533, 542 n.11 (3d Cir. 2022); *Breeze Smoke, LLC v. FDA*, 18 F.4th 499, 506–07 (6th Cir. 2021).

Any doubt on this score is resolved by the FDA's approach to flavored e-cigarettes more generally. Recall that for FDA to prevail, not only must its understanding of the pre-MDO rules be reasonable, but the manufacturers' understanding of those rules also must be *unreasonable. See id.* at 3–4. FDA received over one million PMTAs for flavored e-cigarette products—and not a single one of them contained the scientific studies that FDA now requires and that (it says) any reasonable manufacturer would have known *ex ante* were required. It is perhaps possible that FDA did its part to give the regulated community clear guidance and that one million out of one million not only got it wrong but got it *unreasonably* wrong. But administrative law does not turn on such infinitesimal possibilities. *See Chrysler*, 158 F.3d at 1357. It instead prohibits administrative agencies from saying one thing, pulling a surprise switcheroo, and ignoring the reasonable reliance interests engendered by its previous statements.

E.

Against all of this, FDA's counterargument boils down to this: Some other circuits agree with the agency. It is true that five circuits have sided with FDA, while the Eleventh Circuit and ours have found the agency acted arbitrarily and capriciously. But law is not a nose-counting exercise. *Compare, e.g., Cochran v. SEC*, 20 F.4th 194, 237 (5th Cir. 2021) (en banc) (Costa, J., dissenting) ("Five circuits have considered the question. By a count of 15-0, every judge deciding those cases has [found no jurisdiction.]"), *with Axon Enter., Inc. v. FTC*, 598 U.S. 175, 195–96, 143 S.Ct. 890, 215 L.Ed.2d 151 (2023) (unanimously finding jurisdiction in *Cochran*). Rather, the relevant question is whether our sister circuits have spotted a defect in petitioners' arguments that we have missed. With deepest respect for our colleagues who have seen this case the other way, we think not.

Take for example FDA's principal authority, *Prohibition Juice Co. v. FDA*, 45 F.4th 8 (D.C. Cir. 2022). There the D.C. Circuit rejected the e-cigarette manufacturer's arbitrary-and-capricious claim for two reasons. First, the court of appeals pointed to the June 2019 Guidance, which it read to say "randomized controlled trials or longitudinal studies would not be necessary if applicants submitted similarly rigorous 'valid scientific evidence.' " *Id.* at 21 (quoting June 2019 Guidance at 12, which appears at our A.298). Again, with deepest respect to our colleagues on the D.C. Circuit, that is not what the June 2019 Guidance said. Here is the quoted passage in full:

> The FD&C [Food, Drug, and Cosmetic] Act states that the finding of whether permitting the marketing of a product would be APPH will be determined, when appropriate, on the basis of well-controlled investigations (section 910(c)(5)(A)). However, section 910(c)(5)(B) of the FD&C Act also allows the Agency to consider other "valid scientific evidence" if found sufficient to evaluate the tobacco product. Given the relatively new entrance of ENDS on the U.S. market, FDA understands that limited data may exist from scientific studies and analyses. If an application includes, for example, information on other products (e.g., published literature, marketing information) with appropriate bridging studies, FDA intends to review that information to determine whether it is valid scientific evidence sufficient to demonstrate that the marketing of a product would be APPH. ***387** Nonclinical studies alone are generally not sufficient to support a determination that permitting the marketing of a tobacco product would be appropriate for the protection of the public health.
>
> *Nonetheless, in general, FDA does not expect that applicants will need to conduct long-term studies to support an application.* As an example for nonclinical assessments, long-term studies such as carcinogenicity bioassays are not expected to be included in an application. For clinical assessments, instead of conducting clinical studies that span months or years to evaluate potential clinical impact, applicants could demonstrate possible long-term health impact by including existing longer duration studies in the public literature with the appropriate bridging information (i.e., why the data used are applicable to the new tobacco product) and extrapolating from short-term studies. In addition, nonclinical in vitro assays that assess the toxicities that are seen following long-term use of tobacco products may be supportive of these clinical assessments. These studies, used as a basis to support a PMTA, should be relevant to the new tobacco product and address, with robust rationale, acute toxicological endpoints or other clinical endpoints that may relate to long-term health impacts. In this context, FDA considers long-term studies to be those studies that are conducted over six months or longer.

A.298–99 (emphasis added and footnotes omitted). This passage explicitly states that, instead of performing long-term studies, manufacturers could submit "existing longer duration studies in the public literature with the appropriate bridging information" and "nonclinical in vitro assays that assess the toxicities that are seen following long-term use of tobacco products." A.299.

And it is undisputed that petitioners submitted the specified information. They submitted information from existing studies, along with "bridging" information to connect it to their PMTA products. *See supra*, at 379-81. Neither the D.C. Circuit nor any other court of appeals that has sided with FDA can point to a single word in the June 2019 Guidance (or any other guidance) that says existing data on *unflavored* e-cigarette use is categorically irrelevant to the public health benefits of *flavored* e-cigarettes.

The D.C. Circuit's second explanation is that "FDA nowhere guaranteed that unspecified other forms of evidence would necessarily be sufficient—only that they might be, so the FDA would consider them." *Prohibition Juice*, 45 F.4th at 21. That is true; FDA never guaranteed that any particular study would be sufficient to garner approval of a PMTA. But FDA did tell manufacturers to submit "existing longer duration studies in the public literature with the appropriate bridging

information" and "nonclinical in vitro assays that assess the toxicities that are seen following long-term use of tobacco products." A.299. Petitioners undisputedly submitted those studies. And then FDA turned around and said those studies were *categorically* insufficient because manufacturers should have performed long-term scientific studies of the kind the June 2019 Guidance said were unnecessary.

One of today's dissenting opinions points to a different court of appeals decision—the Fourth Circuit's in *Avail Vapor*. *See post*, at 406-07 (Graves, J., dissenting). In that case, the Fourth Circuit described a PMTA as:

> like a driver's test, in that it has two components: First, valid scientific evidence showing that a product is appropriate for the protection of the public health, like the "written test," and second, ***388** a determination that the totality of the evidence supports a marketing authorization, like the "road test." A marketing plan, which includes youth access restrictions, comes in at the road test phase to support the final determination that an application is appropriate for the protection of the public health.
>
> Like a driver's test, both components are necessary, and neither is sufficient. An applicant who fails the written test does not proceed to the road test. So too here: FDA determined that Avail could not show its products were appropriate for the protection of the public health, and no marketing plan could rectify that baseline infirmity.

Avail Vapor, 55 F.4th at 425.

With greatest respect to our dissenting colleague and our sister circuit, that analogy is misplaced. Unlike a driving test, the statutory text in § 387j(c)(4)(A)–(B) is not disjunctive. The two statutory requirements: "likelihood that existing users of tobacco products will stop using such products" (scientific evidence) and the "likelihood that those who do not use tobacco products will start using such products" (marketing plans) are linked with a conjunctive "and." *Ibid.* The statute does not proceed sequentially; rather, it commands the agency to take *both* criteria into account.

Section 387j(c)(4)(A)–(B) is perhaps better understood as a standardized test with two sections, scored as a composite. Because a low score on part one of a two-part test can be counterbalanced by a high score on the other, the administrator must grade both sections. To put a finer point on it, imagine a hypothetical ENDS product that gets only one existing smoker to quit, but has a marketing plan so restrictive that no non-smokers could access it and use it to start vaping. That product has an obvious net public health benefit. And FDA could not reject a PMTA for it after scoring only half of its test.

In any event, even if the "and" in § 387j(c)(4)(A) could or should be read as "or," that is *still* not enough to save the FDA. As noted, the Eleventh Circuit held the agency repeatedly represented that the marketing plans were "critical" and "necessary" to a successful application. *Bidi Vapor*, 47 F.4th at 1203–04. The agency cannot now claim they were in fact always meaningless.

* * *

In sum, FDA's denials of petitioners' PMTAs were arbitrary and capricious. The agency did not give manufacturers fair notice of the rules; the agency did not acknowledge or explain its change in position; the agency ignored reasonable and serious reliance interests that manufacturers had in the pre-MDO guidance; and the agency tried to cover up its mistakes with *post hoc* justifications at oral argument. The contrary views expressed by some of our sister circuits do not address our principal concerns with FDA's decisionmaking. We therefore hold the agency acted unlawfully.

III.

Finally, FDA argues that even if it arbitrarily and capriciously denied petitioners' applications, that error was harmless. FDA reasons that there is nothing special about petitioners' applications, so the agency will deny them on remand even if we send the case back and order FDA to conform its decisionmaking to the APA. FDA EB Br. 27–28.

FDA misunderstands how harmless error review works under the APA. We (A) explain the harmless error rule and then (B) hold it provides no help to the agency.

***389** A.

In administrative law, the harmless error rule is quite narrow. "It is a well-established maxim of administrative law that if the record before the agency does not support the agency action, or if the agency has not considered all relevant factors, the proper course, except in rare circumstances, is to remand to the agency for additional investigation or explanation."

Calcutt, 598 U.S. at 628–29, 143 S.Ct. 1317 (quotation and citation omitted). "The reviewing court is not generally empowered to conduct a *de novo* inquiry into the matter being reviewed and to reach its own conclusions based on such an inquiry." *Fla. Power & Light Co. v. Lorion*, 470 U.S. 729, 744, 105 S.Ct. 1598, 84 L.Ed.2d 643 (1985). Once we identify an error in the agency's decision, our work is almost always done: If the agency rests its decision on "grounds [that] are inadequate or improper, *the court is powerless* to affirm the administrative action by substituting what it considers to be a more adequate or proper basis."*SEC v. Chenery Corp.* (*Chenery II*), 332 U.S. 194, 196, 67 S.Ct. 1760, 91 L.Ed. 1995 (1947) (emphasis added).

Consider for example *Calcutt.* In that case, FDIC sanctioned the CEO of a bank. The CEO petitioned for review in the Sixth Circuit, and the court of appeals identified two legal errors in the agency's decision. The Sixth Circuit nonetheless held those errors were harmless and denied the CEO's petition. The Supreme Court of the United States unanimously and summarily reversed. *Calcutt*, 598 U.S. at 628, 143 S.Ct. 1317.

Two parts of the *Calcutt* summary reversal bear emphasis. First, the Court emphasized that the "ordinary" rule is that a federal court must remand to the agency as soon as it identifies a legal error in the agency's decision. *Id.* at 629, 143 S.Ct. 1317 ("[T]he Sixth Circuit should have followed the ordinary remand rule here."); *see also Gonzales v. Thomas*, 547 U.S. 183, 187, 126 S.Ct. 1613, 164 L.Ed.2d 358 (2006) (per curiam) (applying "the ordinary remand rule"); *INS v. Orlando Ventura*, 537 U.S. 12, 18, 123 S.Ct. 353, 154 L.Ed.2d 272 (2002) (same). That ordinary remand rule has deep roots in administrative law. Part of it is rooted in the admonition, dating back at least to *Chenery I*, that agency decisions must stand or fall on the explanation the agency gave at the time. Courts are simply not free to look past the error on the supposition that the error would not affect the agency's decisionmaking. And part of it is rooted in the Court's recognition that the Administrative *Procedure* Act requires agencies to follow *procedures*, and those *procedures* are what give agency decisions legitimacy. A court cannot forgive procedural violations simply because the court thinks they did not matter. "[T]he guiding principle, violated here, is that the function of the reviewing court ends when an error of law is laid bare." *FPC v. Idaho Power Co.*, 344 U.S. 17, 20, 73 S.Ct. 85, 97 L.Ed. 15 (1952).

Second, *Calcutt* recognized "[i]t is true that remand may be unwarranted in cases where there is not the slightest uncertainty as to the outcome of the agency's proceedings on remand." 598 U.S. at 629–30, 143 S.Ct. 1317 (quotation omitted). That is a different way of saying remand may be unnecessary where the petitioner could not have been prejudiced. *Shinseki v. Sanders*, 556 U.S. 396, 409, 129 S.Ct. 1696, 173 L.Ed.2d 532 (2009) (requiring courts to consider whether an error was prejudicial); 5 U.S.C. § 706 (same). But, the *Calcutt* Court emphasized, this rule applies "*only in narrow circumstances.*" 598 U.S. at 630, 143 S.Ct. 1317 (emphasis added). Specifically, "[w]here the agency was *required* to take a particular action, ***390** ... that it provided a different rationale for the necessary result is no cause for upsetting its ruling." *Ibid.* (emphasis in original) (quotation and citation omitted). But in any case where the agency's decision was *discretionary*, the ordinary remand rule must apply. *Ibid.* As the *Calcutt* Court put it: The harmless-error "exception does not apply in this case. FDIC was not required to reach the result it did; the question whether to sanction petitioner—as well as the severity and type of any sanction that could be imposed—is a discretionary judgment." *Ibid.* (emphasis omitted).

The upshot: APA errors are only harmless where the agency would be *required* to take the same action no matter what. In all other cases, an agency cannot avoid remand. [7]

7 Of course, an agency cannot *demand* remand where the law is clear and where an agency has failed to heed a prior remand order. *See, e.g., Lewis v. United States*, 88 F.4th 1073, 1079-80 (5th Cir. Dec. 18, 2023); *El Paso Elec. Co. v. FERC*, 76 F.4th 352, 366 (5th Cir. 2023). The principle that unites both lines of precedent is that an administrative agency cannot avoid judicial review by gaming the APA's remand rules.

B.

This case is controlled by *Calcutt.* All agree that FDA's standards for adjudicating PMTAs are discretionary. Those applications are highly fact-specific. And the ultimate decision to approve or deny an application turns on FDA's ever-evolving understanding of what "public health" requires. The harmless-error rule simply does not apply to such discretionary administrative decisions.

Similarly, we have held an "APA deficiency is not prejudicial only when it is one that clearly had no bearing on the

procedure used or the substance of decision reached." *United States v. Johnson*, 632 F.3d 912, 930 (5th Cir. 2011) (quotation and citation omitted). Thus, *Johnson* prohibits us from holding an APA error is harmless simply because the petitioner did not or could not show that but for the error the agency would have decided the matter differently ("the substance of decision reached"). Rather, the rule is stated in the disjunctive, and it provides an error is harmful unless it had "*no* bearing on the procedure used *or* the substance of decision reached." It is hard to imagine an APA error that could have "*no* bearing on the procedure used." And in any event, each of FDA's errors in this case plainly affected "the procedure used" and hence were not harmless. On that score, we agree with the entirety of the Eleventh Circuit's analysis and its application of a harmless error rule identical to *Johnson*'s. *See Bidi Vapor*, 47 F.4th at 1205–08.

* * *

The petitions for review are GRANTED, FDA's marketing denial orders are SET ASIDE, and the matters are REMANDED to FDA.

Haynes, Circuit Judge, joined by Stewart, Southwick, Higginson, and Douglas, Circuit Judges, dissenting:

In 2009, Congress enacted the Family Smoking Prevention and Tobacco Control Act ("TCA"), Pub. L. No. 111-31, 123 Stat. 1776 (2009) (codified at 21 U.S.C. §§ 387–387(u)), to empower the FDA in the fight against tobacco products, which Congress considered "the foremost preventable cause of premature death in America." TCA § 2(13), 123 Stat. at 1777. Concerned that "past efforts to restrict advertising and marketing of tobacco products ha[d] failed adequately to curb tobacco use by ***391** adolescents," TCA § 2(6), 123 Stat. at 1776, Congress submitted authority to the FDA to regulate tobacco products in the interest of public health and, specifically, the protection of our country's youth. *See Big Time Vapes, Inc. v. FDA*, 963 F.3d 436, 444 (5th Cir. 2020) ("Obviously, the TCA's purpose sounds in (1) protecting public health and (2) preventing young people from accessing (and becoming addicted to) tobacco products.").

Over time, e-cigarettes, including "vaping" models, came into play. The notion was that these were safer than regular cigarettes and might get those who are smokers to become vapers and, ultimately, neither. As I discuss more fully below, the e-cigarettes are *not* safe. Just as being shot in the stomach might be less likely to cause death than being shot in the head, but neither one is wanted, neither e-cigarettes nor cigarettes are safe. As such, the focus on e-cigarettes has been to assist those already addicted, not to create a whole new group of youth becoming addicted. Thus, while this dissenting opinion is long, a short sentence could sum it up: the Petitioners here did not establish that their products would so sufficiently assist adults that it would overcome the harm to youth.

As a result of the history of e-cigarettes, as of 2016, e-cigarettes and their component parts (including e-liquids) [1] are subject to the requirements of the TCA. Deeming Tobacco Products To Be Subject to the Federal Food, Drug, and Cosmetic Act, 81 Fed. Reg. 28974 (May 10, 2016) ("Deeming Rule"). The FDA is thus *required* to deny a Premarket Tobacco Product Application ("PMTA") for an e-cigarette unless permitting the product to be marketed would be "appropriate for the protection of the public health" ("APPH"), based on an evaluation of "the risks and benefits to the population as a whole" as demonstrated by "well-controlled investigations" or other "valid scientific evidence." 21 U.S.C. § 387j(c). Contrary to the majority opinion's seeming contention that any application that has some good sounds to it must be granted, the FDA should only be granting anything that is *shown* to aid public health (i.e., the addicted adults), not create more addicted youth such that our country has much earlier deaths over time.

[1] As the majority opinion does, I use the term "e-cigarettes" throughout this opinion to refer to all forms of electronic nicotine delivery devices ("ENDS") and their component parts, including e-liquids.

A body of knowledge growing over the past several years has exposed the extreme risks that flavored e-cigarettes pose to children. By any metric, our country is in the throes of a youth vaping epidemic that has reached crisis proportions. In 2020, 3.6 million kids in the United States reported using e-cigarettes, including 20% of high school students and 5% of middle school students. FDA, *Technical Project Lead (TPL) Review of PMTAs* (2021), at 6. Use of these products at such an early age, "when the developing brain is most vulnerable to nicotine addiction," puts these children at much greater risk of tobacco use and dependence as adults. As the D.C. Circuit noted recently, "[t]he public health consequences are dire: Tobacco is quickly and powerfully addicting, and e-cigarettes can permanently damage developing adolescent brains, cause chronic lung diseases, and hook young users for

life." *Prohibition Juice Co. v. FDA*, 45 F.4th 8, 10 (D.C. Cir. 2022).

Flavored products are a key driver of the problem.[2] According to the 2020 National ***392** Youth Tobacco Survey, 85% of high school e-cigarette users report using a flavored product, compared to 65% in 2014. Petitioners produce e-cigarettes in flavors like sour grape, pink lemonade, and pound cake with names such as "Jimmy The Juice Man Strawberry Astronaut" and "Suicide Bunny Bunny Season"—which, as one member of our sister circuit recently commented, "seem designed to have appeal to kids." *Bidi Vapor LLC v. FDA*, 47 F.4th 1191, 1212–13 (11th Cir. 2022) (Rosenbaum, J., dissenting). Indeed, the FDA has found that the availability of flavored products "is one of the primary reasons for the popularity of [e-cigarettes] among youth."

2 In accordance with the FDA's guidance documents and the parties' briefs, the term "flavored" as used herein does not include tobacco- or menthol-flavored e-cigarettes.

The issue for manufacturers of flavored e-cigarettes, like Petitioners, is that no counterbalancing evidence has emerged as to the product's benefits. While e-cigarettes may help some current smokers quit or switch to vaping, the research does not establish that flavored products provide an increased benefit over non-flavored products. As the FDA noted during its review of Petitioners' PMTAs, "in contrast to the evidence related to youth initiation—which shows clear and consistent patterns of real-world use that support strong conclusions—the evidence regarding the role of flavors in promoting switching among adult smokers is far from conclusive." Thus, according to current knowledge, flavored e-cigarettes present a much higher risk to youth than non-flavored e-cigarettes, without any compensatory benefit. Such a calculus does not bode well for approval under the TCA. Still, in accordance with the guidance it has consistently given applicants, the FDA continues to conduct a case-by-case evaluation of each PMTA for flavored e-cigarettes to determine whether it contains sufficiently reliable and robust evidence to shift the balance of risks and benefits in favor of approval.

It is against this backdrop that the FDA reviewed the PMTAs of Wages and White Lion Investments, LLC, d/b/a Triton Distribution ("Triton") and Vapetasia LLC ("Vapetasia") (collectively, "Petitioners") and issued marketing denial orders ("MDOs") to Petitioners. The FDA denied Petitioners' PMTAs because they did not contain any reliable evidence suggesting the benefits of Petitioners' flavored products outweighed the significant risks to youth—an outcome that aligned with both the guidance the FDA had given to applicants and its statutory mandate under the TCA. But the majority opinion erroneously concludes that the FDA changed the evidentiary standards applied to Petitioners' PMTAs and wholly ignored Petitioners' marketing plans, and thus acted in an arbitrary and capricious manner. Unfortunately, based on a misreading of the law and a misconstruing of the relevant facts, the majority opinion supersedes the FDA's work by remanding instead of denying the petition, which cuts the FDA's legs out from under it in the middle of a dangerous and constantly evolving public health crisis.

In so doing, the majority opinion also departs from all but one of our sister circuits that have addressed the same issue. *See, e.g.*, *Magellan Tech., Inc. v. FDA*, 70 F.4th 622 (2d Cir. 2023) (unanimous denial); *Liquid Labs LLC v. FDA*, 52 F.4th 533 (3rd Cir. 2022) (unanimous denial); *Avail Vapor, LLC v. FDA*, 55 F.4th 409 (4th Cir. 2022) (unanimous denial), *cert. denied*, —— U.S. ——, 144 S.Ct. 277, —— L.Ed.2d —— (2023); *Gripum, LLC v. FDA*, 47 F.4th 553 (7th Cir. 2022) (unanimous denial), *cert. denied*, —— U.S. ——, 143 S. Ct. 2458, 216 L.Ed.2d 431 (2023); *Lotus Vaping Techs., LLC v. FDA*, 73 F.4th 657 (9th Cir. 2023) (unanimous denial); *Prohibition Juice*, 45 F.4th 8 (unanimous denial); *see also* ***393** *Breeze Smoke, LLC v. FDA*, 18 F.4th 499 (6th Cir. 2021) (denying motion for stay), *app. for stay denied*, —— U.S. ——, 142 S. Ct. 638, 211 L.Ed.2d 397 (2021). The only circuit that granted a petition for review in a comparable context did so on much narrower grounds than the majority opinion embraces today. *See Bidi Vapor*, 47 F.4th at 1195 (remanding based on the FDA's failure to consider marketing and sales-access-restriction plans); *but see id.* at 1208–18 (Rosenbaum, J., dissenting). Despite the Eleventh Circuit's opinion, however, it is telling that the Supreme Court recently denied certiorari for two cases in which other circuits considered similar facts to those before us and *denied* the petition for review. *See Gripum, LLC v. FDA*, —— U.S. ——, 143 S. Ct. 2458, 216 L.Ed.2d 431 (2023) (mem.); *Avail Vapor, LLC v. FDA*, —— U.S. ——, 144 S.Ct. 277, —— L.Ed.2d —— (2023) (mem.); *see also Breeze Smoke, LLC v. FDA*, —— U.S. ——, 142 S. Ct. 638, 211 L.Ed.2d 397 (2021) (mem.) (denying application for stay of FDA's denial, without any recorded dissent).

Reevaluating this case en banc, I would reach the same determination that the merits panel did and deny the petitions for review before us. *See Wages & White Lion Invs., L.L.C.*

v. FDA, 41 F.4th 427, 441, 442 (5th Cir. 2022) ("*Wages II*"), *reh'g en banc granted, vacated by*58 F.4th 233 (5th Cir. 2023). Because the majority opinion arrives at a different conclusion, I respectfully dissent.

I. Statutory, Regulatory, and Procedural Background

Before turning to the majority opinion's conclusions, it is worth briefly reviewing the relevant statutory, regulatory, and procedural background of this case.

As previously noted, Congress passed the TCA in 2009 in an effort to protect all Americans, and particularly children, from the health detriments of tobacco. *See, e.g.*, TCA § 2(34), 123 Stat. at 1779 ("Because the only known safe alternative to smoking is cessation, interventions should target all smokers to help them quit completely."); TCA § 2(1), 123 Stat. at 1777 ("The use of tobacco products by the Nation's children is a pediatric disease of considerable proportions that results in new generations of tobacco-dependent children and adults."). Congress decided that the FDA has the necessary "scientific expertise to ... evaluate scientific studies supporting claims about the safety of products[ ] and to evaluate the impact of labels, labeling, and advertising on consumer behavior in order to reduce the risk of harm and promote understanding of the impact of the product on health." TCA § 2(44), 123 Stat. at 1780.

Accordingly, Congress gave broad authority to the FDA to regulate tobacco products, requiring that most "new tobacco product[s]" receive authorization from the FDA prior to marketing. 21 U.S.C. § 387j(a)(2)(A). The TCA applies to "all cigarettes, cigarette tobacco, roll-your-own tobacco, and smokeless tobacco" as well as "any other tobacco products that the [FDA] Secretary by regulation deems to be subject to this subchapter." *Id.* § 387a(b). In 2016, the FDA used that discretion to deem e-cigarettes as tobacco products subject to the requirements of the TCA. Deeming Rule, 81 Fed. Reg. 28974.

Under the Deeming Rule, manufacturers must submit PMTAs to the FDA for any flavored e-cigarettes and their component parts, such as the e-liquids manufactured by Petitioners. The majority opinion is a switcheroo from the statute: the TCA *requires* the FDA to *deny* any PMTA if the applicant cannot show that marketing such a tobacco product "would be appropriate for the protection of the public health [APPH]." 21 U.S.C. § 387j(c)(2)(A). ***394** In determining whether a product is APPH, the FDA must consider "the risks and benefits to the population as a whole." *Id.* § 387j(c)(4). This includes considering "the increased or decreased likelihood that existing users of tobacco products will stop using such products," *id.* § 387j(c)(4)(A), as well as "the increased or decreased likelihood that those who do not use tobacco products will start using such products," *id.* § 387j(c)(4)(B). The FDA must make this determination "on the basis of well-controlled investigations" or other "valid scientific evidence" that, in the FDA's discretion, is "sufficient to evaluate the tobacco product." *Id.* § 387j(c)(5). Thus, the FDA must use its science to evaluate the applications and cannot grant an insufficient PMTA.

Although the Deeming Rule was set to go into effect in August 2016, various events pushed out its final deadline until September 2020. In the intervening years, more information came to light regarding the prevalence of and dangers associated with e-cigarette use, particularly by youth. In case there were any doubts about the deleterious effects of e-cigarettes, research into the use of such devices has made several things clear: (1) e-cigarette usage entails myriad health risks, including lifelong addiction to e-cigarettes or traditional cigarettes, lung disease, and attention and learning deficits; (2) in most instances the use of, and addiction to, tobacco products begins during adolescence; and (3) e-cigarettes are the most popular tobacco product among youth, with flavored e-cigarettes having particular appeal.

E-cigarettes thus pose a significant public health risk, particularly to children. Concerningly, the FDA observed a "dramatic increase in the prevalence of [e-cigarette] use among U.S. youth in 2018," which caused the FDA Commissioner to label the problem a "youth vaping epidemic." The FDA responded by increasing enforcement efforts, particularly against non-tobacco and non-menthol flavored e-cigarettes. In 2020, the FDA issued a guidance document announcing its new priorities and describing the underlying evidence showing that flavors were a key driver of increased youth use of e-cigarettes. FDA, "Enforcement Priorities for Electronic Nicotine Delivery Systems (ENDS) and Other Deemed Products on the Market Without Premarket Authorization" ("January 2020 Guidance"). [3]

3 The majority opinion suggests that the January 2020 Guidance "did not apply to [P]etitioners or their liquids" because "Petitioners do *not* make e-cigarettes, vape pens, vape pods, vape cartridges or any other vaping device covered by the January

> 2020 Enforcement Guidance," but then cites to the January 2020 Guidance as evidence of FDA's positions on the public health standard as applied to e-cigarettes. Like the majority opinion, I find value in the January 2020 Guidance as an expression of the FDA's views on topics relevant to its assessment of whether Petitioners' products were APPH, particularly regarding the heightened risk that flavored products pose to kids. The January 2020 Guidance focused on closed-system devices, which generally come with prefilled e-liquid cartridges that are replaced after the e-liquid runs out, whereas Petitioners market flavored e-liquids that can be used to refill open-system products. However, in response to the FDA's increased enforcement efforts against flavored closed-system devices, youth responded by migrating to other device types that also had flavored e-liquids. Specifically, "when FDA changed its enforcement policy to prioritize pod-based flavored ENDS, which were most appealing to youth at the time, [it] subsequently observed a substantial rise in use of disposable flavored [e-cigarettes]—a ten-fold increase (from 2.4% to 26.5%) among high school current e-cigarette users." Thus, the FDA identified the "fundamental role of flavor" of any kind in driving youth appeal to e-cigarettes.

On September 9, 2020, Petitioners submitted PMTAs to the FDA seeking permission to market various flavored e-cigarette products. In September 2021, the ***395** FDA reviewed these PMTAs and issued MDOs to Petitioners. As to Triton, the FDA explained the "key basis" for its denial was that its "PMTAs lack[ed] sufficient evidence demonstrating that [its] flavored [e-cigarettes] will provide a benefit to adult users that would be adequate to outweigh the risks to youth." Vapetasia received a similar explanation. The FDA further elaborated on its reasoning in technical project lead reports ("TPLs") it provided to Petitioners.

Petitioners timely sought review of the FDA's denials in our court. Triton moved for a stay, and the two cases were consolidated for appeal. A motions panel granted Triton's motion for a stay in October 2021, *Wages & White Lion Invs., L.L.C. v. FDA*, 16 F.4th 1130, 1144 (5th Cir. 2021) ("*Wages I*"), before a merits panel denied the petitions for review in July 2022, *see Wages II*, 41 F.4th at 442. Petitioners subsequently submitted petitions for panel rehearing and rehearing en banc. The merits panel denied the petition for panel rehearing by equal vote,[4] before we ordered the case be reheard en banc.

4 By the time all of this came into play, one of the members of the merits panel who had joined in the majority opinion had resigned from our court. Thus, the merits panel had only the original author of the majority opinion and the author of the dissenting opinion who, unsurprisingly, did not agree.

II. The FDA Did Not Act Arbitrarily and Capriciously

Our duty in this case is to determine whether the FDA's denials of Petitioners' PMTAs were "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." *See*21 U.S.C. § 387*l*(b); 5 U.S.C. § 706(2)(A). The scope of our review is very narrow. *Motor Vehicle Mfrs. Ass'n of U.S., Inc. v. State Farm Mut. Auto. Ins.*, 463 U.S. 29, 43, 103 S.Ct. 2856, 77 L.Ed.2d 443 (1983). Critically, "[i]t is not our job as a reviewing court to redo an agency's evaluation of relevant evidence." *Avail Vapor*, 55 F.4th at 427. We are "not to substitute [our] judgment for that of the agency" and must "uphold a decision of less than ideal clarity if the agency's path may reasonably be discerned." *FCC v. Fox Television Stations, Inc.*, 556 U.S. 502, 513, 129 S.Ct. 1800, 173 L.Ed.2d 738 (2009) (quotations omitted).

The majority opinion takes issue with two aspects of the FDA's review: (1) the evidentiary standards applied to Petitioners' PMTAs, and (2) the FDA's approach towards Petitioners' marketing plans. Both were reasonable exercises of the agency's authority.

A. Evidentiary Standards

Unlike every other circuit that has ruled on this issue,[5] the majority opinion concludes that the FDA changed the evidentiary ***396** standards it applied to flavored e-cigarettes between the pre-MDO guidance and the denials of Petitioners' PMTAs. In reality, however, the FDA consistently communicated the evidentiary standard that it would apply to all PMTAs for flavored e-cigarettes, applied that standard to Petitioners' PMTAs, and rightfully concluded that Petitioners' applications did not meet it and thus must be denied—all in accordance with its mandate under the TCA.

5 *See Magellan Tech.*, 70 F.4th at 630 ("Given that the FDA did not impose a new evidentiary standard on Magellan, the FDA did not need to provide notice or consider its reliance interests" and thus "the FDA did not act arbitrarily or capriciously."); *Liquid Labs*, 52 F.4th at 541 ("[T]he FDA did not 'reverse course' and newly require randomized controlled trials and/or longitudinal cohort studies, and therefore did not upset Liquid Labs' reliance interests, provide inadequate notice, or act arbitrarily and capriciously."); *Avail Vapor*, 55 F.4th at 421 ("[W]e join the majority of our sister circuits in finding that FDA neither changed the standard nor the types of evidence required."); *Breeze Smoke*, 18 F.4th at 507 ("[T]he FDA's 2019 language and its 2021 order likely did not fail to consider reliance interests, ... and did not introduce a new standard of review in adjudication such that it likely deprived Breeze Smoke of fair warning."); *Gripum*, 47 F.4th at 560 (agreeing with Sixth Circuit and D.C. Circuit that FDA did not shift its evidentiary standard); *Lotus Vaping Techs.*, 73 F.4th at 673 ("[T]he agency consistently advised that, in the absence of long-term data, it might rely upon sufficiently robust and reliable other evidence" and "did not act arbitrarily or capriciously by concluding that Petitioners' evidence fell short of that standard."); *Prohibition Juice*, 45 F.4th at 20 ("We hold that the FDA did not misdirect applicants."). Even the Eleventh Circuit's decision in *Bidi Vapor* was limited to consideration of the FDA's approach to the marketing and sales-access-restriction plans, and the opinion did not address the FDA's position on evidentiary requirements for PMTAs. *See Bidi Vapor LLC*, 47 F.4th at 1195 (holding limited to consideration of marketing and sales-access-restriction plans).

1. Pre-MDO Communications

First and foremost, the FDA consistently communicated that it would conduct a case-by-case determination of each PMTA pursuant to the standard mandated by the TCA. *See* 21 U.S.C. § 387j(c) (PMTAs must present "well-controlled investigations" or other "valid scientific evidence" showing that "permitting such tobacco product to be marketed would be appropriate for the protection of the public health"); *see also* FDA, Premarket Tobacco Product Applications and Recordkeeping Requirements, Proposed Rule, 84 Fed. Reg. 50566, 50619 (Sept. 25, 2019) ("September 2019 Proposed Rule") ("FDA will determine ... whether the available evidence, when taken as a whole, is adequate to support a determination that permitting the new tobacco product to be marketed would be APPH."). Each guidance documented cited by the majority opinion makes clear that the recommendations contained therein extend only insofar as they further the statutory requirements. *See, e.g.*, FDA, Premarket Tobacco Product Application Content Overview (Oct. 23, 2018), https://perma.cc/BV8D-HR7H ("October 2018 Guidance") at 3–5, 31–32 (outlining statutory requirements); FDA, Premarket Tobacco Product Application (PMTA) Review Pathway, at 20 (Oct. 28, 2019), https://perma.cc/9S7Z-JQX8 ("October 2019 Guidance") at 5–6 (same); FDA, "Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems: Guidance for Industry" ("June 2019 Guidance") at 10 ("FDA will review an ENDS PMTA consistent with the requirements of section 910(c) of the FD&C Act."); FDA, Press Release, FDA Makes Significant Progress in Science-Based Public Health Application for Review, Taking Action on Over 90% of More than 6.5 Million 'Deemed' New Tobacco Products Submitted (Sept. 9, 2021), https://perma.cc/4F69-MRUB ("As we have said before, the burden is on the applicant to provide evidence to demonstrate that permitting the marketing of their product meets the applicable statutory standard."). As such, any suggestion that the FDA was required to accept evidence it deemed unsatisfactory under the TCA requirements "neglect[s] the forest for the trees." *See Avail Vapor*, 55 F.4th at 419.

In advance of the September 2020 deadline, as the FDA continued to gather more information about youth e-cigarette use, the agency made clear that the bar of "valid scientific evidence" was a high one. The FDA issued a document containing "Nonbinding Recommendations" [6] in June ***397** 2019 that stated, "[n]onclinical studies alone are generally not sufficient to support a determination that permitting the marketing of a tobacco product would be appropriate for the protection of the public health." June 2019 Guidance at 12; *see also id.* at 34 (same). However, "in some cases, it may be possible to support a marketing order for an ENDS product without conducting new nonclinical or clinical studies," such as "if there is an established body of evidence regarding the health impact (individual or population) of [the] product or a similar product that can be adequately bridged to [the] product." *Id.* at 46. In order to demonstrate APPH, the June

2019 Guidance also recommended "an applicant compare the health risks of its product to both products within the same category and subcategory, as well as products in different categories as appropriate." *Id.* at 13. As such, the FDA made clear that evidence of comparisons between flavored and non-flavored e-cigarette products was a recommended part of a PMTA.

6 The majority opinion suggests that, although it is "unquestionably true that the pre-MDO guidance documents had all manner of disclaimers, qualifiers, and cautionary language," the FDA cannot "deny that it changed its position based on th[at] qualified language." As detailed herein, the evidentiary standards that the FDA applied to Petitioners' PMTAs align with the pre-MDO guidance, so the FDA did not change its position. The conditional language used by the FDA in its nonbinding guidance documents indicates that it never guaranteed that a certain type of evidence would be sufficient. This is a reasonable position, particularly in such a rapidly evolving area of public health concern. The cases cited by the majority opinion are inapposite. *See Physicians for Soc. Resp. v. Wheeler*, 956 F.3d 634, 646 (D.C. Cir. 2020) (explaining the EPA fully acknowledged it had changed its position and that the point of contention was whether EPA sufficiently acknowledged the reasons underlying its change in course); *Southwest Airlines Co. v. FERC*, 926 F.3d 851, 858 (D.C. Cir. 2019) (holding that "the Commission's ***consistent practice***, whether adopted expressly in a holding or established impliedly through repetition, sets the baseline from which future departures must be explained" (emphasis added)).

Notably, although the FDA never required (and still does not require) any specific type of study, it also never said that nonclinical studies *would be* sufficient to support a PMTA. Rather, the FDA has always suggested and continues to suggest that such studies might be useful, in particular where, as here, the evidence presented in a PMTA is otherwise weak. *See, e.g.*, October 2018 Guidance ("[I]t *may be* possible to support a marketing order for an ENDS product without conducting new nonclinical or clinical studies given other data sources can support the PMTA." (emphasis added)); June 2019 Guidance at 13 ("In addition, nonclinical in vitro assays that assess the toxicities that are seen following long-term use of tobacco products *may be* supportive of these clinical assessments." (emphasis added)), 12 (FDA "intends to review" non-clinical evidence), 47 ("Published literature reviews (including meta-analysis) or reports *may be* acceptable to support a PMTA, but are considered a less robust form of support for a PMTA." (emphasis added)); Premarket Tobacco Product Applications and Recordkeeping Requirements (Final Rule), 86 Fed. Reg. 55300, 55387 (Oct. 5, 2021) ("FDA *does not expect* that long-term clinical studies will need to be conducted for each PMTA; instead, it *expects* that it should be able to rely on other valid scientific evidence to evaluate some PMTAs." (emphasis added)). Ultimately, while the FDA "broadened the types of evidence it would consider" beyond just randomized controlled trials or longitudinal studies, it also "made clear it would not relax the scientific rigor of the requisite public health demonstration." *Prohibition Juice*, 45 F.4th at 21.

***398** To summarize, leading up to the September 2020 deadline, the FDA published nonbinding guidance to give applicants an insight into what the PMTA review would look like, namely: (1) a case-by-case assessment, (2) guided first and foremost by statutory requirements, with (3) the burden on applicants to provide (4) valid scientific evidence (likely in the form of randomized control trials or longitudinal studies, although other forms of similarly robust and reliable evidence *may be* sufficient) (5) showing that the public health benefits of their specific products outweighed the risks.

2. Application to Petitioners' PMTAs

Then, the FDA applied that standard to Petitioners' applications. The FDA considered whether Petitioners' PMTAs demonstrated "potential benefits to smokers from marketing [the] products with robust and reliable evidence" that was "significant enough to overcome the risk to youth." Because flavored e-cigarettes present a disproportionately high risk to children, the risk to youth was higher for Petitioners' products than for similar menthol- or tobacco-flavored e-cigarettes. The FDA rightfully factored that into its review by examining whether the applications had "any acceptably strong evidence that the flavored products have an added benefit relative to that of tobacco-flavored ENDS in facilitating smokers completely switching away from or significantly reducing their smoking."

The FDA reasonably concluded Petitioners did not submit sufficiently robust and reliable scientific evidence to demonstrate the requisite benefit. [7] According to Petitioners'

PMTAs, "[t]he most important consideration in deciding whether e-cigarettes produce a public health benefit is determining if using e-cigarettes is an effective cessation method for combustible cigarette use." Both Petitioners submitted a variety of published studies and articles discussing topics relevant to the APPH determination. However, Petitioners admitted their own literature reviews found "not enough evidence from well-designed studies to determine whether e-cigarette flavors aid in smoking cessation."

7 This appeal was filed more than two years ago. At the time it was filed, the Petitioners contended they were not given the time to do the studies the FDA sought. Thus, they originally asked this court alternatively to "vacate the MDOs and enjoin FDA from taking further adverse action on Petitioners' PMTAs for 18 months if Petitioners will be required to conduct long-term studies to demonstrate comparative efficacy going forward." Given that this case and the "18 month request" were filed more than two years ago, Petitioners now have had plenty of time. Indeed, during that time, they could have reapplied to the FDA with whatever information they gathered. Yet, to my knowledge, and based on the lack of any information to the contrary from the Petitioners, the Petitioners have submitted no additional evidence during that time to the FDA. Given the majority opinion's remand, the Petitioners certainly will not have an argument about a lack of time.

Vapetasia also submitted a cross-sectional survey as part of its PMTA, which the FDA similarly found did not change the risk-benefit balance. The panel opinion summarized why that was a reasonable conclusion:

> [The] survey suffered from several methodological flaws: (1) only 294 people were surveyed; (2) the survey respondents are all Vapetasia customers; and (3) it's not clear how these individuals were selected to take the survey.[ ] In other words, there were strong reasons to doubt the survey's results. The FDA therefore did not act arbitrarily in concluding that Vapetasia's survey "is not sufficient to show a benefit to adult smokers."

***399** *Wages II*, 41 F.4th at 436 (footnote omitted).

In both Petitioners' MDOs, the FDA explained that this evidence was not sufficient to make the requisite showing under the TCA:

> All of your PMTAs lack sufficient evidence demonstrating that your flavored ends will provide a benefit to adult users that would be adequate to outweigh the risks to youth. In light of the known risks to youth of marketing flavored ends, robust and reliable evidence is needed regarding the magnitude of the potential benefit to adult smokers. This evidence could have been provided using a randomized controlled trial and/or longitudinal cohort study that demonstrated the benefit of your flavored ends products over an appropriate comparator tobacco-flavored ends. Alternatively, FDA would consider other evidence but only if it reliably and robustly evaluated the impact of the new flavored vs. Tobacco-flavored products on adult smokers' switching or cigarette reduction over time. We did not find such evidence in your PMTA[s]. Without this information, FDA concludes that your application is insufficient to demonstrate that these products would provide an added benefit that is adequate to outweigh the risks to youth and, therefore, cannot find that permitting the marketing of your new tobacco products would be appropriate for the protection of the public health.

The FDA provided an additional explanation for Vapetasia:

> Although your PMTAs contained a cross-sectional survey "Vapetasia PMTA Survey and Testimonial", this evidence is not sufficient to show a benefit to adult smokers of

> using these flavored ENDS because it does not evaluate the specific products in the application(s) or evaluate product switching or cigarette reduction resulting from use of these products over time.

The FDA thus reasonably concluded that, as compared to menthol- and tobacco-flavored products, Petitioners' flavored products posed an increased risk in seducing children to start vaping without any evidence of a heightened benefit in helping existing smokers quit. Accordingly, as the FDA said in its briefing, "FDA denied petitioners' applications *not* because they failed to include a randomized controlled trial or longitudinal cohort study but because they failed to include *any* evidence robust enough to carry petitioners' burden under the statute." This outcome is not only reasonable but required under the TCA. *See*21 U.S.C. § 387j(c).

3. The FDA's Position Has Not Changed

So, where is the switch? The FDA's denials of Petitioners' PMTAs are a product of the same standards that the FDA shared with applicants before the September 2020 deadline and has continued to publicize since then. None of the FDA's communications or actions since September 2020 indicate otherwise.

The majority opinion suggests that the FDA announced a new "scientific-studies-or-bust standard" in an August 2021 press release that said:

> Based on existing scientific evidence and the agency's experience conducting premarket reviews, the evidence of benefits to adult smokers for such products would likely be in the form of a randomized controlled trial or longitudinal cohort study, although the agency does not foreclose the possibility that other types of evidence could be adequate if sufficiently robust and reliable.

***400** *See* FDA, Press Release, FDA Denies Marketing Applications for About 55,000 Flavored E-Cigarette Products for Failing to Provide Evidence They Appropriately Protect Public Health (Aug. 26, 2021), https://perma.cc/LCD8-VWGQ ("Aug. 2021 Press Release"). Setting aside that the FDA has always centered its guidance on the statutory requirement for "valid *scientific* evidence," this statement is simply not a deviation from the guidance quoted above. According to its experience and expertise, the FDA believed randomized control trials or longitudinal cohort studies were most likely to provide persuasive enough evidence of benefits to adult smokers that would outweigh the high risk to youth of flavored e-cigarettes, but it was willing to consider other data if sufficiently robust and reliable. This approach aligns with the TCA and all of the FDA's pre-MDO communications.

The majority opinion faults the FDA for failing to give fair notice that "FDA will deny your application if you do not conduct long-term studies on your specific flavored product." But the FDA has never imposed a requirement for long-term studies, much less a requirement for those studies conducted on Petitioners' specific products. As demonstrated above, the FDA did not reject Petitioners' applications because they lacked a certain type of study on any certain type of product, but rather because they lacked "*any* evidence robust enough to carry petitioners' burden under the statute."

The majority opinion also says that "[i]n its explanation for denying petitioners' applications, FDA imposed two requirements—randomized controlled trials and longitudinal cohort studies." But even a cursory read of the MDO belies that portrayal:

> In light of the known risks to youth of marketing flavored ends, robust and reliable evidence is needed regarding the magnitude of the potential benefit to adult smokers. This evidence could have been provided using a randomized controlled trial and/or longitudinal cohort study that demonstrated the benefit of your flavored ends products over an appropriate comparator tobacco-flavored ends. Alternatively, ***FDA would consider other evidence but only if it reliably and robustly***

> ***evaluated the impact of the new flavored vs. Tobacco-flavored products on adult smokers' switching or cigarette reduction over time***.

Contrary to the majority opinion's assertion, this last line cannot possibly be code for a randomized control trial or longitudinal cohort study because it is explicitly presented as an "alternat[e]" option. Nor is this a requirement for long-term scientific studies; rather, it is an emphasis on evidence regarding long-term *impact.* As our sister circuits have stated:

> [T]he "FDA never guaranteed that manufacturers could carry their evidentiary burden under the [Act] without providing long-term data." ... And by focusing on isolated statements in the 2019 Guidance that the FDA did not expect applicants would need to conduct long-term studies, Petitioners "failed to look at the 2019 guidance in any depth," as "[t]he agency made quite clear that it was interested in receiving information about long-term *impact*, even if that information did not necessarily come from a long-term *study*."

Lotus Vaping Tech., 73 F.4th at 672 (quoting *Avail Vapor*, 55 F.4th at 422–23 (brackets in original)).

Indeed, the FDA's interest in long-term impact is rooted in the statutory APPH standard, which requires FDA to consider "the increased or decreased likelihood that existing users of tobacco products will stop using such products." ***401** 21 U.S.C. § 387j(c)(4)(A). As we explained in the panel opinion, "[n]othing can 'increase' or 'decrease' in a vacuum." *Wages II*, 41 F.4th at 434. Accordingly, although the FDA imposed no long-term studies requirement, it did emphasize the importance of valid scientific evidence demonstrating long-term impact, which should not have come as a shock to anyone given the comparative efficacy requirements in the TCA. [8]

8 The majority opinion states that "there is no question that petitioners compared the health risks of their products to other products as the June 2019 Guidance recommended," pointing to this quote from the FDA's en banc brief:
> Petitioners asserted in their application that "flavors are crucial to getting adult smokers to make the switch and stay away from combustible cigarettes," ... that adult smokers prefer flavored e-cigarettes to tobacco-flavored e-cigarettes, ... and that this preference "has powerful implications for not only the role of flavors in helping smokers' transition from smoking to vaping, but also in connection with helping vapers maintain smoking abstinence and preventing relapse to smoking."
Petitioners' "assert[ions]" are a far cry from valid scientific evidence. Furthermore, even cherry-picking findings from individual studies with no mention of the methodological concerns cannot refute Petitioners' own conclusion that "there is not enough evidence from well-designed studies to determine whether e-cigarette flavors aid in smoking cessation." In other words, the fact that Petitioners presented other scientific evidence in their PMTAs does not mean that such evidence was valid or persuasive. Similarly, just because Petitioners included some "bridging" information in an attempt to connect existing studies about unflavored products to their own flavored products does not mean that evidence was sufficient—indeed, the FDA apparently concluded it was not.

Nor does the FDA's denial of all PMTAs it has thus far received for flavored e-liquids indicate that the FDA changed its position. The majority opinion frames this as a "categorical ban" on flavored e-liquids, which it sees as dispositive evidence that the FDA changed its position without fair notice to Petitioners. But this was a case-by-case review (so we should not review ones not before us) and, as stated before, the FDA is not obligated to *grant* but rather obligated to *deny UNLESS* the e-cigarette in question would benefit the adult health well over the harm to the youth health. Thus, there is another more likely explanation: none of these applications had sufficient evidence that their products were APPH ***because flavored e-liquids are not APPH***. That is, the high risk that these products in particular pose to youth—including increased likelihood of starting to use nicotine and tobacco products, becoming addicted, and experiencing other health problems including permanent damage to developing brains—is not outweighed by the benefit they may provide in helping adult smokers quit. [9]

9 No applicant has submitted reliable evidence to the contrary. As mentioned above, the Petitioners have now had plenty of time to get more information but have not, at least based upon the information in our court, bothered to do so.

Of course, it is not the court's role to make this determination. Congress has provided that authority to the FDA. [10] Drawing on its scientific expertise (far greater than ours), the FDA has evaluated each PMTA for flavored e-liquids individually and concluded it did not provide sufficient ***402** evidence to demonstrate its product was APPH. The agency presumably will continue this case-by-case evaluation, remaining open to the possibility that a PMTA for a flavored e-liquid product could provide sufficiently robust and reliable evidence to tip the APPH balance in favor of approval, unless and until it announces a change in its position. [11] But the FDA is not required to approve an unsatisfactory application to market a flavored e-liquid just to prove that it has not imposed a categorical ban on these products—in fact, it is prohibited by the statute from doing so. *See*21 U.S.C. § 387j(c).

10 Contrary to the majority opinion's assertion, it is also neither our nor the FDA's responsibility to "say what 'other evidence' petitioners might have supplied to win approval." As detailed herein, both the statute and the FDA's guidance provide recommendations for what types of valid scientific evidence might be sufficient. But the statute places the burden on ***applicants*** to present such evidence showing their product is APPH, and it requires the FDA to deny any PMTA that fails to do so. *See*21 U.S.C. § 387j(c)(2)(A).

11 The majority opinion's statement that a "categorical ban" would have "other statutory problems," including requiring adherence to notice-and-comment obligations, underscores the point that the FDA has never imposed such a ban.

The majority opinion's portrayal of Petitioners' PMTA denials as a categorical ban on the use of data involving unflavored products in flavored-product PMTAs similarly ignores the facts of this case and the APPH balancing standard mandated by the TCA. The FDA consistently advised applicants that data regarding other products should only be included in a PMTA to the extent it is appropriate to show the product at issue is APPH. *See, e.g.*, October 2018 Guidance at 11 (advising that, if a PMTA "[c]ompare[s] the new tobacco product to a representative sample of tobacco products on the market," it should "[i]nclude justification for why using evidence or data from other products is appropriate"); June 2019 Guidance at 48 (advising applicants who rely on literature reviews to "[p]rovide adequate justification for bridging data from the new product studied to your new product"). Further, as the FDA was acutely aware, the risks associated with flavored products are higher than those associated with non-flavored products, which means evidence of benefits for flavored products must be stronger than for non-flavored products to satisfy the APPH standard. *See*21 U.S.C. § 387j(c)(2) and (4). That necessarily suggests evidence about the benefits of non-flavored products, by itself, would not be sufficient for the FDA to approve a PMTA for a flavored product. Nevertheless, as promised, the FDA continues to conduct a case-by-case assessment of each PMTA, including whether an applicant has presented sufficiently robust "bridging" evidence justifying its use of other products' data. Based on the FDA's scientific expertise, Petitioners simply failed to do so here. [12]

12 Remember, even Petitioners admitted their own literature reviews found "not enough evidence from well-designed studies to determine whether e-cigarette flavors aid in smoking cessation"—a glaring admission to which the majority opinion provides no response.

In this case, Petitioners failed to show that their products were APPH. As our sister circuits have held, "[t]he Agency's finding that the evidence was insufficiently rigorous does not reflect a changed standard, but the manufacturers' failure to meet the standard the agency consistently applied." *Prohibition Juice*, 45 F.4th at 21; *see also Lotus Vaping Techs.*, 73 F.4th at 673 ("[W]e join the Second, Third, Fourth, Seventh, and D.C. Circuits in determining that the agency consistently advised that, in the absence of long-term data, it might rely upon sufficiently robust and reliable other evidence. The agency did not act arbitrarily or capriciously by concluding that Petitioners' evidence fell short of that standard."). Because "FDA did not 'reverse course' and newly require randomized controlled trials and/or longitudinal cohort studies," we should safely conclude that it "did not upset [Petitioners'] reliance interests ... or act arbitrarily and capriciously" ***403** and deny the petitions. *Liquid Labs LLC*, 52 F.4th at 541.

B. Marketing Plans

The majority opinion also concludes that the FDA acted arbitrarily and capriciously because it entirely failed to consider Petitioners' sales and marketing plans in its review of their PMTAs, but the record demonstrates that is not the case.

In their PMTAs, Petitioners included summaries of their marketing plans, which provided that their products "w[ould] continue to be strictly marketed and sold to adults in adult-only retailers and through age-verified online websites," and that Petitioners and third parties would not promote these products "on social media, radio or television." Petitioners also averred that they would use "robust age-verification software," such as "a pop-up 'age-gate.' " As part of these age-verification measures, Petitioners also described their implementation of "AgeCheckner.Net ... which provides state-of-the-art age verification services to online stores that sell age restricted products such as vaporizers and tobacco related products."

In its MDOs and TPLs to Petitioners, the FDA explained that it had reviewed Petitioners' PMTAs, and that its "assessment includes evaluating the appropriateness of the proposed marketing plan[s]." However, in a footnote, the FDA also discussed the fact that, "to date, none of the [e-cigarette] PMTAs that the FDA has evaluated have proposed advertising and promotion restrictions that would decrease appeal to youth to a degree significant enough to address and counter-balance the substantial concerns ... regarding youth use." Accordingly, the FDA stated, "for the sake of efficiency, the evaluation of the marketing plans in applications will not occur at this stage of review, and we have not evaluated any marketing plans submitted with these applications."

As the record makes clear, the FDA was not mistaken in its approach to Petitioners' sales and marketing plans. The FDA determined that it would not fully consider Petitioners' marketing plans in light of the fact that, although "[i]t is theoretically possible that significant mitigation efforts could adequately reduce youth access and appeal," it had not once evaluated a marketing plan that actually did so. This conclusion accords with guidance the FDA published in 2020, which noted that youth use of e-cigarettes continued to rise despite the FDA's prior efforts to curb predatory marketing. Based on its expertise, the FDA determined that traditional marketing schemes like those Petitioners submitted—which rely on customers self-verifying their age at the point of sale—are inadequate to prevent young people from starting to use e-cigarettes. Indeed, the FDA explained that, based on "the most recent data that youth use of [e-cigarette] products continues to increase," it "believes that age verification alone is not sufficient to address this issue," and "focusing on how the product was sold would not be sufficient to address youth use of these products." In contrast, the FDA has pointed to proposed plans that use "biometric locking mechanism[s]" to prevent youth use as an example of "novel" marketing plans that could adequately address youth access.

The majority opinion characterizes the FDA as having effectively misled applicants, including Petitioners, as to the potential significance that marketing plans would play in the agency's review of PMTAs. However, this description is at odds with the aforementioned guidance, which provides readers with clear insight into the FDA's data-backed determination that traditional marketing schemes are inadequate ***404** to stem the tide of youth misuse of e-cigarettes. *See Prohibition Juice Co.*, 45 F.4th at 25 (highlighting where petitioners' "plans—to require customers' self-verification of age at the point of sale and to use what they characterize as less vibrant marketing unappealing to youth—track measures the FDA in its 2020 guidance deemed inadequate"); *Lotus Vaping Techs.*, 73 F.4th at 674 (reviewing FDA's 2020 Guidance in the context of petitioners' marketing plan challenge and noting FDA's conclusion that, based on the inadequacies of manufacturers' proposed measures to restrict youth access to e-cigarettes, efforts related to how e-cigarette products are sold are insufficient to deter youth use).

It is certainly true that the FDA previously acknowledged that marketing plans are a relevant factor to its overall review of PMTAs. *See*Premarket Tobacco Product Applications and Recordkeeping Requirements (Proposed Rule), 84 Fed. Reg. 50566, 50581 (Sept. 25, 2019) ("The applicant's marketing plans will help FDA determine whether permitting the marketing of the new tobacco product would be [appropriate for the protection of public health]"); Premarket Tobacco Product Applications and Recordkeeping Requirements (Final Rule), 86 Fed. Reg. 55300, 55324 (Oct. 5, 2021) ("FDA has rationally concluded that the required descriptions of marketing plans will directly inform ... its consideration of the potential impact on youth initiation and use."). However, these acknowledgments do not obviate the clear "Guidance for Industry" the FDA provided in 2020 that traditional marketing plans would be inadequate for purposes of PMTAs. Put differently, what the FDA made clear through its various announcements was that marketing plans were *necessary* for PMTAs, but traditional marketing plans were not *sufficient* to justify approval of such applications. This is a particularly salient distinction in the context of flavored e-cigarettes, where an incremental decrease in the alarmingly high risk to youth cannot compensate for the utter lack of evidence of the product's benefits.

If the FDA had not actually reviewed *any* documentation regarding the content of the marketing plans, the FDA arguably could not have known that Petitioners' plans aligned with the traditional, ineffective plans and were not unique. But that is not the case here. Rather, the FDA clarified at oral argument that it *did* review summaries of Petitioners' marketing plans contained within their PMTAs, and thus reasonably concluded that Petitioners' plans contained no novel proposals that would have changed FDA's analysis. *See Wages II*, 41 F.4th at 441.

Of course, we do not accept post hoc justifications for agency actions, and the FDA "must defend its actions based on the reasons it gave *when it acted*." *Dep't of Homeland Sec. v. Regents of the Univ. of Cal.*, —— U.S. ——, 140 S. Ct. 1891, 1909, 207 L.Ed.2d 353 (2020) (emphasis added). But the FDA's explanation at oral argument is not the same as a situation in which an agency submits an *entirely new*, post hoc argument for why a previous action was justified. On the contrary, in its MDOs and TPLs, the FDA explained that its "evaluation of the marketing plans in applications will not occur at this stage of review" only after *separately* stating that its "assessment [of PMTAs] includes evaluating the appropriateness of the proposed marketing plan." The FDA had clearly stated that it reviewed the PMTA; that document clearly includes a summary of the marketing. Within the context of these two, at-first-seemingly contradictory stances, the FDA's oral argument statements are not a newly fabricated post hoc justification but instead a *clarification* of ***405** the FDA's approach to reviewing marketing materials (i.e. reviewing the marketing plan summaries rather than the full marketing plans themselves).

This clarification is not inconsistent with the FDA's explanations in the MDOs and TPLs, and the panel opinion properly considered it. Indeed, this is exactly the type of factual clarification we seek at oral argument. *See, e.g., Cooper Cameron Corp. v. U.S. Dep't of Lab., OSHA*, 280 F.3d 539, 542 (5th Cir. 2002) ("Given the gaps in the record, we attempted to clarify at oral argument what kinds of documents OSHA had withheld ... Counsel for the DOL, to his credit, conceded that the withheld material included some newspaper articles."); *Schofield v. Saul*, 950 F.3d 315, 322 (5th Cir. 2020) (noting that counsel at oral argument asserted the agency had not relied on the decision of the appeals council, so the panel declined to consider it); *Pennzoil Co. v. FERC*, 789 F.2d 1128, 1139 & n.28 (5th Cir. 1986) (relying on FERC counsel's responses to questions at oral argument when concluding that the FERC Commissioner decided the case at issue on procedural grounds).[13] Other circuit courts facing cases similar to this have also taken into consideration the explanations and other concessions made during oral arguments. *See, e.g., Avail Vapor, LLC*, 55 F.4th at 425 (discussing the FDA's explanation "in oral argument" that "a PMTA is like a driver's test, in that it has two components"); *Bidi Vapor LLC*, 47 F.4th at 1208 (distinguishing the case before the court with this case while noting that "the statements made before the Fifth Circuit at oral argument by the [FDA] ... were not made before this Court").

13 The majority is correct that none of these cases stands for the proposition that an agency can use oral argument to provide post hoc rationalizations that contradict its past positions; that is because, as we clearly state herein, an agency is not permitted to do so. *See Regents of the Univ. of Cal.*, 140 S. Ct. at 1909. But the FDA did not do that in this case. Here, the FDA made two seemingly contradictory express statements in the record: first, it said that it reviewed the PMTA, which included a summary of the marketing plan; then, it said that it did not evaluate any marketing plan submitted with the application during its review. The oral argument comments simply clarified this point.

Common sense makes clear that we must be able to consider these types of clarifications—otherwise, we should have far fewer oral arguments. Put simply, we are free, and indeed often choose, to ask questions of agencies during oral argument and account for their answers that are consistent with or explain the evidence. This process allows us to ground our conclusions in the most-accurate facts of a given case. Doing so here makes clear that the FDA's approach to Petitioners' marketing plans was not arbitrary and capricious.

* * *

The facts of this case and the applicable law, as confirmed by our sister circuits, make the conclusion in this case clear: the FDA properly fulfilled its statutory mandate by considering the relevant portions of Petitioners' PMTAs and coming to a reasonable conclusion that marketing Petitioners' products is not appropriate for public health. Because the majority comes to a different conclusion, I respectfully dissent.

James E. Graves, Jr., Circuit Judge, joining the dissent in part:

I agree with the dissent that the FDA did not act arbitrarily or capriciously when it denied Petitioners' Premarket Tobacco Product Applications. I also agree with most, but not all, of the dissent's analysis. I write separately as to the FDA's treatment ***406** of Petitioners' sales and marketing plans.

In determining "whether the marketing of a tobacco product ... is appropriate for the protection of the public health," the FDA must consider (A) the "increased or decreased likelihood that existing users of tobacco products will stop using such products" and (B) "the increased or decreased likelihood that those who do not use tobacco products will start using such products." 21 U.S.C. § 387j(c)(4)(A)–(B). It is the applicant's burden to demonstrate to the FDA that its product meets that standard. § 387j(c)(2)(A); *see supra* at 393. As to part (B) in this case, Petitioners were required to submit a marketing plan to explain to the FDA how they would avoid attracting new or youth tobacco users. *See, e.g.*, 84 Fed. Reg. 50581.

I fully agree with the dissent that the FDA correctly concluded that Petitioners failed to present any satisfactory evidence as to part (A). The issue, then, is whether the FDA acted arbitrarily and capriciously by failing to consider the marketing plans that Petitioners submitted to satisfy part (B). The majority concludes that the FDA did not consider the plans, and that its decision not to do so was arbitrary and capricious. The dissent concludes that the FDA *did* consider the plans, and that the FDA's experience with, and data about, similar marketing plans was a sufficient basis on which to deny them.

The majority correctly concludes that the FDA did not consider the marketing plans to any significant degree. The FDA told Petitioners as much when it denied their applications, writing that "for the sake of efficiency, the evaluation of the marketing plans in applications will not occur at this stage of review, and we have not evaluated any marketing plans submitted with these applications."

The dissent concludes that the FDA clarified at oral argument that it reviewed summaries of Petitioners' marketing plans, and from the summaries could tell that the plans were inadequate. I agree that this court may, and often does, seek clarification at oral argument. But the FDA's statement does not clarify. Among other things, the statement raises the question of why, if the FDA did review the summaries, it told Petitioners that it had "not evaluated any marketing plans." As it stands, the FDA's statement at oral argument is at odds with the record. For that reason alone, the court should disregard it.

Nor can I agree that the FDA would have been justified to "not fully consider" the marketing plans because its data and experience showed that traditional marketing schemes, generally, are not adequate to curb youth access to e-cigarettes. Just because no applicant has introduced a satisfactory marketing scheme does not mean that one cannot exist. Moreover, as the dissent notes, 21 U.S.C. § 387j(c)(2) sets forth a framework for case-by-case analysis of applications. While general scientific understanding of the dangers of flavored tobacco products will no doubt inform the FDA's consideration of each application, the agency also must not reject a marketing plan on the basis that it judged some other plans to be deficient.

In my view, however, the FDA correctly declined to evaluate the marketing plans. It appears that only the Eleventh and Fourth Circuits have reached the merits of this issue. The Eleventh Circuit concluded that the FDA's decision not to review the plans was arbitrary and capricious because the FDA represented that the plans were "critical" and "necessary." *Bidi Vapor LLC v. FDA.*, 47 F.4th 1191, 1203-04 (11th Cir. 2022).

The Fourth Circuit reached the opposite conclusion. It analogized:

> ***407** [A Premarket Tobacco Product Application] is like a driver's test, in that it has two components: First, valid scientific evidence showing that a product is appropriate for the protection of the public health, like the "written test," and second, a determination that the totality of the evidence supports a marketing authorization, like the "road test." A marketing plan, which includes youth access restrictions, comes in at the road test phase to support the final determination that an application is appropriate for the protection of the public health.
>
> Like a driver's test, both components are necessary, and neither is sufficient. An applicant who fails the written test does not proceed to the road test. So too here: FDA determined that Avail could not show its products were appropriate for the protection of the public health, and no marketing plan could rectify that baseline infirmity.

Avail Vapor, LLC v. FDA, 55 F.4th 409, 425 (4th Cir. 2022).

That analogy is apt because part (A) and part (B) are "pass-fail" tests—an applicant either satisfies them or it does not—that are bound by the conjunctive "and," such that each represents a "critical" and "necessary" showing that is nevertheless insufficient on its own to carry an applicant's burden.

The majority poses a hypothetical involving an application for an e-cigarette product "that gets only one existing smoker to quit, but has a marketing plan so restrictive that no non-smokers could access it and use it to start vaping." *Supra* at p. 388. The majority reasons that such a product would seemingly score poorly on part (A) of the test, but that because of its obvious public health benefit, the FDA "could not reject a PMTA for it." *Id.* But that hypothetical fails to capture the essence of § 387j(c)(2), which concerns long-term "risks" and "likelihoods" and is necessarily predictive. When an applicant submits its application, no one knows for certain whether its product will cause one smoker or 100,000 smokers to quit smoking; the best an applicant can do is present scientific evidence to aid the FDA in making a prediction. If an applicant furnishes enough evidence to support "the increased ... likelihood that existing users of tobacco products will stop using such products," part (A) is satisfied. If not, the applicant fails part (A), and consequently, the larger test.

Here, Petitioners failed to submit reliable evidence that their products provide any benefit to adult smokers. Once the FDA made that determination, Petitioners' marketing plans, and any other aspect of part (B), became irrelevant, because even the most promising plans would not have helped them show that their products are appropriate for the protection of the public health. For that reason alone, the FDA's decision not to review the plans was justified. There was no error.

In sum, the FDA did not act arbitrarily or capriciously when it denied Petitioners' applications.

All Citations

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